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Robotic surgery of the pancreas

Daniel Joyce, Gareth Morris-Stiff, Gavin A Falk, Kevin El-Hayek, Sricharan Chalikonda, R Matthew Walsh

Daniel Joyce, Gareth Morris-Stiff, Gavin A Falk, Kevin El-Hayek, Sricharan Chalikonda, R Matthew Walsh, Department of General Surgery, Digestive Disease Institute, Cleveland Clinic, Cleveland, OH 44195, United States

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Correspondence to: Daniel Joyce, Resident Physician, Department of General Surgery, Digestive Disease Institute, Cleveland Clinic, Cleveland, OH 44195, United States. joyced4@ccf.org

Telephone: +1-216-4457576 Fax: +1-216-4457653

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Core tip: This invited article reviews the latest developments in robotic surgery of the pancreas in a clear and succinct manner. It highlights the merits of robotic surgery while explaining the challenges that physicians face when integrating new technology into clinical practice.

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Abstract

Pancreatic surgery is one of the most challenging and complex fields in general surgery. While minimally invasive surgery has become the standard of care for many intra-abdominal pathologies the overwhelming majority of pancreatic surgery is performed in an open fashion. This is attributed to the retroperitoneal location of the pancreas, its intimate relationship to major vasculature and the complexity of reconstruction in the case of pancreatoduodenectomy. Herein, we describe the application of robotic technology to minimally invasive pancreatic surgery. The unique capabilities of the robotic platform have made the minimally invasive approach feasible and safe with equivalent if not better outcomes (*e.g.*, decreased length of stay, less surgical site infections) to conventional open surgery. However, it is unclear whether the robotic approach is truly superior to traditional laparoscopy; this is a key point given the substantial costs associated with procuring and maintaining robotic capabilities.

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INTRODUCTION

Pancreatic surgery remains one of the most challenging and complex fields in general surgery. Kausch^[1] performed the first pancreatoduodenectomy (PD) in 1909, with the operation later being popularized by Dr. Allen Oldfather Whipple, though he only performed 37 such operations in his career. Nevertheless, the operation did not gain widespread acceptance until the 1980s having gained notoriety as a dangerous and morbid operation, which was associated with a 30% perioperative mortality rate^[2]. The centralization of pancreatic surgery to high volume referral centers has led to a reduction in the perioperative mortality rate to less than 5% for PD^[2-5]. Despite improvements in technique and perioperative care, major pancreatic resections carry an appreciable rate of major morbidity with high volume centers reporting a 30%-40% morbidity rate for PD^[3-5].

Minimally invasive surgical approaches are becoming the standard of care for many abdominal operations given their superiority over open procedures in terms of surgical site infection, postoperative pain, and length of stay while providing equivalent oncologic outcomes in

cases of malignancy^[6]. The laparoscopic approach is now considered the standard of care for cholecystectomy, anti-reflux surgery, colon cancer, and bariatric surgery. It is worthwhile considering the concept of surgical oncotaxis in patients with pancreatic cancer, one of the most aggressive solid organ malignancies. This concept proposes that surgical stress can depress the anti-tumor immune response and foster tumor progression^[7]. Kondo *et al*^[8] demonstrated a reduction in the incidence of systemic inflammatory response in patients undergoing minimally invasive PD. In addition, earlier and improved recover may lead to more patients receiving adjuvant therapies or being enrolled into clinical trials.

It is now almost twenty years since Gagner and Pomp^[9] described the first laparoscopic PD, however, it has not gained widespread popularity. This has been attributed to the retroperitoneal location of the pancreas, its close relationship with major vascular structures, and the tedious nature of the dissection required to optimize oncological margins in pancreatic cancer. Perhaps the largest barrier of all to laparoscopic PD is the challenge of reconstruction since three separate anastomoses are required. This is illustrated by the more widespread acceptance of distal pancreatectomy (DP) in recent years since there is no reconstruction required^[10]. However, the laparoscopic approach to DP may itself be under-utilized^[11]. The slow adoption of minimally invasive pancreatic surgery, particularly PD, mirrors that of prostatectomy. Laparoscopic prostatectomy never gained popularity due to its technical complexity and steep learning curve, reported to be in the range of 150 cases, when assessed in terms of blood loss and operating time. In fact, it may require a staggering 700 cases to reach expert proficiency in maximizing potency outcomes in patients undergoing prostatectomy^[12]. In 2001, prostate surgery was revolutionized by the introduction of the robotic surgery. In less than eight years, robotic assisted prostatectomy has become the most common approach to prostatectomy in the United States with over 60% of prostatectomies being performed with robotic assistance^[13].

The development of robotic surgery was spurred by an interest in the military to perform operations remotely such as near the battlefield, or in space^[14]. While much of the early work was completed by the US Department of Defense, the current and only robotic surgery platform has been brought to the marketplace by Intuitive Surgical®. The DaVinci® surgical system consists of a three or four-armed robot which is operated by the surgeon who sits at a separate console. The robotic platform overcomes many of the key shortcomings of traditional laparoscopy that include monocular vision, limited degrees of freedom and the effects of pivot and fulcrum, which make suturing in particular difficult to master. In contrast, the robotic approach affords the surgeon a three-dimensional stereoscopic view of the operating field and restores hand-eye coordination that is often lost in traditional laparoscopy when the camera is offset to the plane of dissection. Endowrist®

(Sunnyvale, CA) instrumentation not only replicates the movements of the human hand with seven degrees of freedom but also eliminates hand tremor (Figure 1A). The key triumph of the robotic platform over traditional laparoscopy is the ease with which one can suture and tie intracorporeal knots independent of the operative setup. The robotic approach is not without disadvantages. The lack of haptic feedback has been cited as a possible drawback since its absence may lead surgeons to place excessive tension whilst tying sutures leading to tearing of the tissues being sutured^[15]. The robotic platform is expensive with an initial capital cost of \$1-2.5 million; annual maintenance liabilities well over \$100000, and many of the instruments are single use only^[16].

This review discusses the impact of robotic technology on pancreatic minimally invasive surgery.

ROBOTIC PANCREATODUODENECTOMY

Giulianotti *et al*^[17] first performed robotic assisted PD in 2001, and the initial series of 8 patients demonstrated that robotic PD was feasible and safe, reporting a 37.5% morbidity rate and one perioperative death (due to Boerhaave's Syndrome). The mean operative time in this series was 270 min. Surgeons have adopted robotic assistance for minimally invasive PD with much more enthusiasm than the traditional laparoscopic approach. Indeed the authors of the first reported laparoscopic PD series concluded at one point that there was no benefit to the minimally invasive approach to PD^[10,18]. In 2012 it was reported that only 7 centers worldwide had an experience of 30 or more patients who had undergone laparoscopic PD^[19], somewhat meager progress for an operation initially described eighteen years earlier.

On the contrary, robotic assisted PD while not widespread is being reported with increasing frequency. This mirrors the development of minimally invasive prostatectomy; robotic assistance seems to act as an enabler to surgeons who do not feel comfortable performing the operation with conventional laparoscopic techniques. The reported approaches for robot assisted PD vary, some groups adopt a hybrid laparoscopic/robotic approach while others perform the entirety of the operation robotically. Narula *et al*^[20] report a hybrid laparoscopic and robotic approach for PD, the authors complete the dissection laparoscopically and employ the robot to perform the reconstruction taking advantage of the precision and dexterity of the robot for placing sutures (Figure 1B). Fernandes *et al*^[21], the initial pioneers of the robotic PD advocates a full robot-assisted approach believing that "there is no role for a hybrid hand-assisted or laparoscopic/robotic approaches".

It is reasonable to conclude that robot assisted PD is a safe operation and can be performed with a rate of morbidity and mortality equivalent to open PD. Several series demonstrate a reduction in blood loss and a trend towards reduced length of stay (LOS) *vs* the open operation, for example the most recent series published

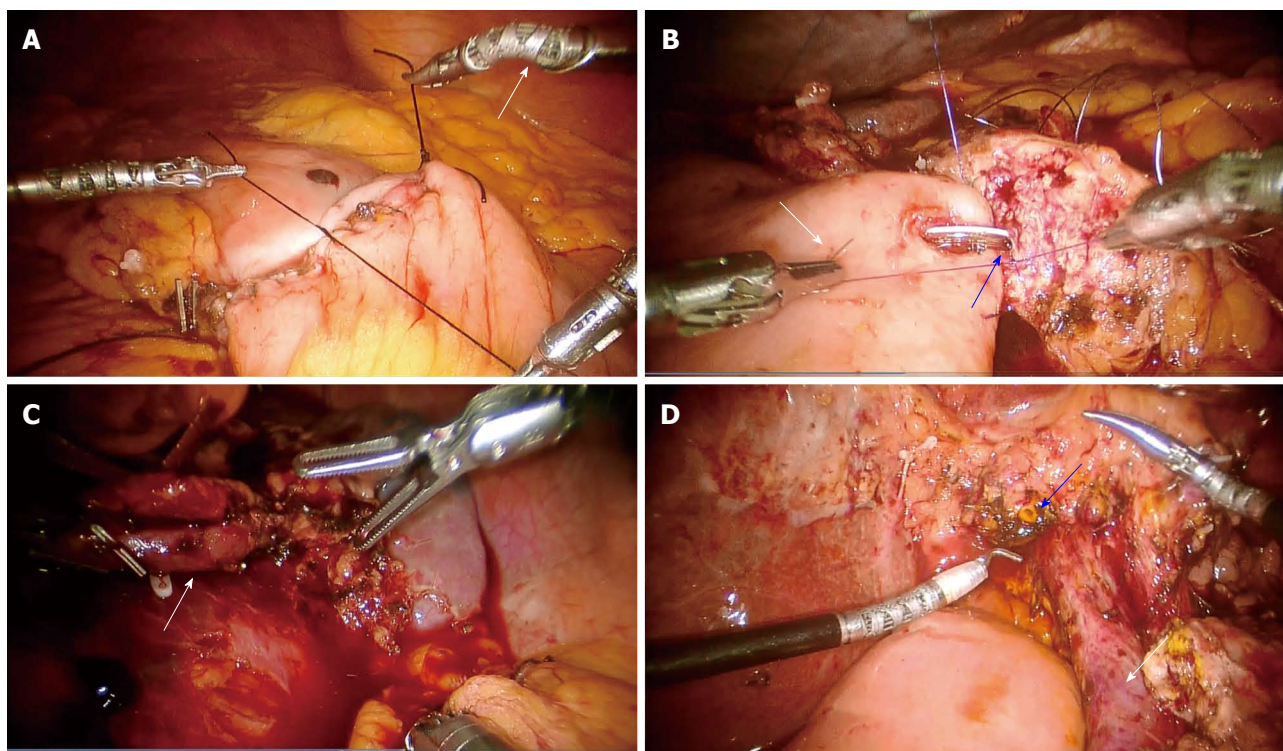


Figure 1 Robotic surgery of the pancreas. A: Completion of the second layer of the anterior duodenojejunal anastomosis following pancreatoduodenectomy. The white arrow highlights the endowrist® capabilities of the robotic arms; B: Completion of the posterior row of the pancreaticojejunal anastomosis with intracorporeal knot tying. The white arrow indicates the jejunal limb with the blue arrow pointing to a pediatric feeding tube entering the main pancreatic duct; C: Splenic hilum following robotic spleen preserving distal pancreatectomy. The excellent visualization and advanced endowrist® technology allow for a precise dissection of the splenic artery and vein (white arrow); D: Hepatic hilum (common hepatic duct indicated by blue arrow, portal vein indicated by white arrow) following resection of pancreatic head and duodenum.

describes the operation in 132 patients with a mean EBL of 527 mL and an average LOS of ten days. Comparative studies detailing open PD *vs* the robotic approach report reduced blood loss with the latter approach^[22-24]. PD is an operation associated with morbidity rates of 30%-50%; robotic surgery appears at least equivalent to open surgery in terms of morbidity and mortality. A recent meta-analysis of robotic *vs* open pancreatectomy favored the robotic approach with a risk difference of 12% for morbidity between open and robotic approaches^[25]. Of course, one has to be mindful that many of the studies involved may have a selection bias favoring the robotic approach, with surgeons choosing small and more favorable periampullary tumors for cases early in their robotic series. That said, these tumors are often found within the setting of a soft pancreas and a small duct, and thus pancreatic fistulae may be expected more commonly in these patients. Furthermore, the robotic approach may lead to surgery being performed in patients with a high body mass index that previously may have not been considered for an open approach. The morbidity of PD is largely driven by the incidence of pancreatic fistula. Once again the robotic approach compares favorably with contemporary series of open PD, with rates varying from 6%-35% (Table 1). However, the data must be interpreted with caution since the definition of the presence and severity of pancreatic fistulae is not uniform across published

reports, moreover some of the initial series did not perform a pancreaticojejunostomy and opted for pancreatic duct closure.

PD is primarily performed for periampullary and pancreatic carcinomas hence the oncologic outcome of the resection is a key measure by which one should judge the success of one approach over the other. All series report acceptable rates of a microscopically negative “R0” resection (80%-100%), and an adequate lymph node harvest. The systematic review by Cirocchi *et al*^[26] included thirteen case series with an average R1 resection rate of 9%. Another systematic review reported a greater lymph node harvest with the minimally invasive approach to PD^[27]. These impressive results must be interpreted with caution since many surgeons tend to opt for the open approach in patients with larger more extensive tumors while preferring the robotic approach in patients with more oncologically favorable ampullary and duodenal malignancies. It is also important to consider the new staining techniques used to assess resection margins, in particular the retroperitoneal margin, as these now show that R0 rates are less than previously accepted, and hence future series will need to use this methodology so that accurate comparisons of oncological benefits of robotic surgery may be assessed^[28].

In summary robot assisted minimally invasive approach to PD appear to lead to a reduction in operative

Table 1 Outcomes of robot assisted pancreatoduodenectomy

Ref.	n	OR time (mean)	EBL (mean)	LOS (mean)	RO	LN harvest (mean)	Conversion	Fistula	Morbidity	Mortality
Giulianotti <i>et al</i> ^[40]	60	421	394	22 (5-85)	Italy: 100% United States: 89%	Italy: 21 United States: 15	18%	31.30%	NR	1.5% ¹
Buchs <i>et al</i> ^[46]	41	431.5	389	12.7	NR	NR	4.80%	19.50% (4A/3B/1C)	39%	2.40%
Narula <i>et al</i> ^[20]	5	420	NR	9.6	NR	16	37.50%	0	NR	0%
Zhou <i>et al</i> ^[24]	8	718	153	16.4	100%	NR	0%	25%	NR	0%
Zeh <i>et al</i> ^[47]	50	568	350	10	89%	18	16%	20% (5A/2B/4C)	26% I / II 30% III / IV	2%
Chalikonda <i>et al</i> ^[22]	30	476	485	9.79	100%	13.2	10%	6.60%	30%	3%
Lai <i>et al</i> ^[23]	20	491.5	247	13.7	73.30%	10	5%	35%	50%	0%
Zureikat <i>et al</i> ^[36]	132	527	NR	10	NR	NR	8%	17% (12A/5B/5C)	41% I / II 22% III / IV	30 d: 2% 90 d: 5%

¹Included other pancreatic cases. NR: Not recorded; LOS: Length of stay; EBL: Estimated blood loss; LN: Lymph node; OR: Operating.

blood loss and reduced length of hospital stay. In addition, the approach appears equivalent to open surgery in terms of short-term oncologic outcome, and both morbidity as well as mortality. However, these outcomes must be interpreted carefully given the retrospective nature of the data and the real possibility of selection bias in favor of those patients considered for the robotic approach to PD.

ROBOTIC DISTAL PANCREATECTOMY

Laparoscopic distal pancreatectomy (DP) has been adopted with much more enthusiasm than PD; this is unsurprising since there is no reconstruction involved. It can be performed safely and affords the patients several advantages including less blood loss, fewer complications, less pain and a reduced length of stay^[22,29] (Table 2). A multicenter comparative study evaluated 142 laparoscopic and 200 open DPs, demonstrating less blood loss for the laparoscopic technique (357 mL *vs* 588 mL), an overall reduction in complications (40% *vs* 57%), and a reduced LOS (5.9 d *vs* 9 d)^[30]. Nonetheless the laparoscopic approach may be limited by a lower spleen preservation rate and a higher rate of unplanned splenectomy^[31]. Others cite concern for the oncological adequacy of laparoscopic DP given the reduced dexterity associated with the laparoscopic approach. Despite the acceptance of laparoscopic DP in the literature it has not been widely applied; NSQIP data for 2005-2010 reports that 27% of DP cases are performed laparoscopically^[11].

The robotic approach to distal pancreatectomy is also gaining popularity. Daouadi *et al*^[32] reported on a retrospective series of robotic and laparoscopic DPs (30 *vs* 94 respectively), the results were significant for a reduced conversion rate to open surgery (0% *vs* 16%), a trend toward fewer incomplete resections (non R0 resections), and a shorter operative time (293 min *vs* 371 min). This is in contrast however to the majority of reports which report a longer operative time for robotic DP^[26]; this may be explained by the groups extensive experience with the robotic approach.

Splenic preservation is indicated for benign and low-grade pancreatic tumors; the benefits of which are highly significant with a reduction in infectious and overall complications^[33] (Figure 1C). Two groups have demonstrated high rates of splenic preservation with the robotic approach; Hwang *et al*^[34] successfully preserved the spleen in 21 of 22 cases (95.5%), and the Indiana University group reported splenic preservation rates of 65%, 12% and 29% for robotic DP, laparoscopic DP and open DP respectively^[35] in a retrospective series with unspecified selection criteria. This paper also reported a reduced LOS for the robotic group (3.8 d) as compared to 7.7 and 6.4 d for the open and laparoscopic groups respectively, the savings associated with this leading to the robotic approach being comparable from a cost standpoint.

The morbidity of robotic DP is at least equivalent to its open and laparoscopic counterparts. Zureikat *et al*^[36] reported a 43% (27A, 10B, 4C) pancreatic fistula rate in a series of 83 patients undergoing robotic DP. Other groups report lower fistula rates with the meta-analysis performed by Cirrochi *et al*^[37] reporting a 16.9% fistula rate, however, not all groups reported pancreatic fistulae according to the ISGPF definition. Minimally invasive DP is also associated with a lower surgical site infection rate in comparison to the open approach; this of course is not exclusive to the robotic approach and applies equally to the traditional laparoscopic approach^[38].

In summary, robot assisted DP is indeed feasible and safe with distinct advantages over open surgery including a reduced length of stay and overall complication rate. Additionally the rate of splenic preservation appears to be far superior to the open and laparoscopic approach. However, it is questionable if the robotic approach affords the patient additional advantages over traditional laparoscopic DP particularly when splenic preservation is not indicated.

OTHER PROCEDURES

While malignancy remains the most frequent reason for pancreatic surgery, many patients undergo resection or

Table 2 Outcomes of robot assisted distal pancreatectomy

Ref.	n	OR time (mean)	EBL	LOS (mean)	Conversion	Fistula	Morbidity	Mortality
Waters <i>et al</i> ^[35]	17	298	279	4	12%	0	18%	0
Kang <i>et al</i> ^[48]	20	298	372	7.18	NR	NR	10%	0
Daoudi <i>et al</i> ^[32]	30	293	212	6.1	0	46% (6A/4B/4C)	46% I/II	0
Giulianotti <i>et al</i> ^[40]	46	331	323	9.3	6.5%	20.9%	20% III/IV	NR
Zureikat <i>et al</i> ^[46]	83	256	NR	6	2%	43% (22A/10B/4C)	60%	0

NR: Not recorded; LOS: Length of stay; EBL: Estimated blood loss; LN: Lymph node; OR: Operating.

drainage procedures for chronic pancreatitis. The benefits of a robotic approach may be even more applicable to this cohort of patients who have a benign disease and are primarily undergoing surgery to ameliorate pain and improve their quality of life. The major resectional procedures have been discussed in detail above.

The versatility of the robotic platform is illustrated by a series of case reports documenting less common procedures in patients with chronic pancreatitis. Peng *et al*^[39] reported four cases of robot-assisted duodenum preserving pancreatic resection while Zureikat *et al*^[36] reported three Frey procedures. There have also been reports of successful robotic Puestow procedures with Fernandes *et al*^[21] reporting on eight patients who underwent the operation with resolution of pain in 80% of patients, and a 0% anastomotic fistula rate. Giulianotti *et al*^[40] have reported a case of robotic assisted PD with preservation of the vascular supply for autologous islet cell transplantation. The authors reported dissection of the pancreas whilst maintaining arterial supply and venous drainage *via* the gastroduodenal artery and the superior pancreaticoduodenal vein^[40]. Another group reported the first robotic total pancreatectomy with auto islet transplantation, again preserving blood supply until the final moments before specimen removal^[41]. While these reports describe uncommon procedures and do not carry statistical weight, they do illustrate the versatility of the robotic platform in particular its utility in performing intricate vascular dissections.

DISCUSSION

The pancreas, in particular the head of the gland continues to be a relatively unexplored territory in terms of laparoscopic pancreatic resection. There are of course a few pioneers who have conquered the learning curve, but it is a challenge for the average surgeon to achieve. Robotic technology assists the surgeon in overcoming many of the obstacles that render the totally laparoscopic approach unfeasible. The superior visualization (Figure 1D) and restoration of hand-eye coordination along with the increased dexterity allowed by the robotic platform seems to empower even a moderate volume surgeon to complete complex pancreatic resection and reconstruction with at least equivalent results to the open approach with an acceptable learning curve. The minimally invasive approach as described above is associated with a reduc-

tion in blood loss, a reduced length of stay and perhaps a reduction in overall complications. There is however no difference in the rate of post-operative pancreatic fistula or mortality. Oncologic outcomes in selected patients appear equivalent and perhaps better than open surgery in terms of margin status and lymph node harvest but long-term outcomes are as yet unknown. Future studies should not only monitor long-term oncologic outcomes but also the outcomes of surgery such as adhesive bowel obstruction, incisional hernia formation and chronic pain. Such data will inform the risk to benefit profile of each individual operation, this is particularly important for patients undergoing pancreatic resection for pre-malignant disease *e.g.*, IPMN and indeed for those patients undergoing surgery for pancreatic cancer as improved systemic therapies lead to long term survival.

One may argue that robotic assistance may not improve outcomes beyond the standard minimally invasive approach, for example the use of the robot in laparoscopic colon and rectal surgery has not proven superior to standard laparoscopy^[42]. This may be indeed be the case in DP, however, the use of the robot seems to make minimally invasive PD a safe and realistic option whereas many surgeons felt totally laparoscopic PD was not a feasible option with traditional laparoscopic instruments.

Robotic surgery is commonly criticized for the costs involved. Robotic prostatectomy was the first robotic operation to gain widespread acceptance across the surgical community, notwithstanding this several groups have reported that it is not cost effective despite reduced morbidity and length of stay^[43,44]. There are sparse cost data available for robotic pancreatic surgery, however, two groups have reported that the higher costs associated with the robotic approach were offset by a reduction in the length of stay^[34,45]. The cost of the robotic approach may also be offset by a quicker return to economic productivity by the patient and reduction in the long-term effects associated with laparotomy. Intuitive Surgical® holds a monopoly on robotic surgical technology but one can anticipate future competition, which will lead to a reduction in cost.

In summary, it is rational to conclude that robotic pancreatic surgery is feasible and safe in an environment where surgeons and support staff are appropriately trained. One must bear in mind that the published results originate from high volume specialist centers and may not apply to lower volume practitioners, furthermore

the possibilities of patient selection and publication bias are real. It is not clear whether the robotic approach affords the patient and society a net benefit both in terms of “cure” and overall cost. The natural solution to this impasse would be to perform a randomized control trial to define the clinical utility of the robotic approach *vs* traditional approaches. Like many technological innovations it is likely that the surgical community will adopt the technology before such robust evidence is furnished. Given the unlikelihood of a fully powered randomized controlled trial we must continue to scrutinize outcomes particularly long-term oncologic outcomes. In this changing healthcare environment it is likely that both government and third party payers will demand data that supports the superiority of new technologies such as the robot given the substantial equipment costs.

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