Review Article

Short-term and long term morbidity in robotic pancreatic surgery: a systematic review

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Background: Pancreatic cancer is one of the most aggressive and lethal tumours in Western society. Pancreatic surgery can be considered a challenge for open and laparoscopic surgeons, even if the accuracy of gland dissection, due to the close relationship between pancreas, the portal vein, and mesenteric vessels, besides the reconstructive phase (in pancreaticoduodenectomy), lead to significant difficulties for laparoscopic technique. Minimally invasive pancreatic surgery changed utterly with the development of robotic surgery. However, this review aims to make more clarity on the influence of robotic surgery on long-term morbidity.

Methods: A systematic literature search was performed in PubMed, Cochrane Library, and Scopus to identify and analyze studies published from November 2011 to September 2020 concerning robotic pancreatic surgery. The following terms were used to perform the search: "long term morbidity robotic pancreatic surgery".

Results: Eighteen articles included in the study were published between November 2011 and September 2020. The review included 2041 patients who underwent robotic pancreatic surgery, mainly for a malignant tumour. The two most common robotic surgical procedures adopted were the robotic distal pancreatectomy (RDP) and the robotic pancreaticoduodenectomy (RPD). In two studies, patients were divided into groups; on the one hand, those who underwent a robotic pancreaticoduodenectomy (RPD), on the other hand, those who underwent robotic distal pancreatectomy (RDP). The remaining items included surgical approach such as robotic middle pancreatectomy (RMP), robotic distal pancreatectomy and splenectomy, robotic-assisted laparoscopic pancreatic dissection (RALPD), robotic enucleation of pancreatic neuroendocrine tumours.

Conclusions: Comparison between robotic surgery and open surgery lead to evidence of different advantages of the robotic approach. A multidisciplinary team and a surgical centre at high volume are essential for better postoperative morbidity and mortality.

Keywords: Robotics; pancreatic surgery; comorbidity; technique; pancreatic fistula

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Introduction

Pancreatic cancer is one of the most aggressive and lethal tumours in Western society (1). However, despite the advances in oncological therapy, the only chance of cure for patients with this disease is surgery to remove macroscopic and microscopic diseases (R0). Unfortunately, due to distant metastasis or locally invasive disease at the time of the diagnosis, only a few patients with pancreatic cancer are candidates for surgical therapy (2). The median disease-free survival time following complete resection and adjuvant chemotherapy is about 13–14 months (3). Approximately 19% of pancreatic cancer

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patients survive one year after diagnosis and 4% for five years, making this disease so lethal (4).

Nevertheless, surgery could be considered the cornerstone of multidisciplinary treatment that combines the benefit of surgery, chemotherapy, and radiotherapy to achieve the best results (2). Pancreatic surgery can be considered a challenge for open and laparoscopic surgeons, even if the accuracy of gland dissection, due to the close relationship between pancreas, the portal vein, and mesenteric vessels, besides the reconstructive phase (in pancreaticoduodenectomy), lead to significant difficulties for laparoscopic technique. Minimally invasive pancreatic surgery changed utterly with the development of robotic surgery, in particular since the introduction of the Da Vinci robotic platform (Intuitive Surgical, Sunnyvale, CA, USA). The robotic approach provides a three-dimensional stereoscopic view of the operating field; also, Endowrist instruments mimic the human hand's movements with seven degrees of freedom, removing hand tremor and improving the precision of dissection and suturing (1,5). For these reasons, the literature suggests many reports on minimally invasive robotic-assisted pancreatic surgery in the last years. The safety and oncologic efficacy of this approach is still doubtful, as well as the knowledge of outcomes of patients who underwent robotic pancreatic surgery.

This review aims to summarize the current literature about robotic pancreatic surgery and underline which are the short-term and long-term morbidity comparing robotic surgery with the laparoscopic and open approach.

We present the following article in accordance with the PRISMA reporting checklist (available at http://dx.doi.org/10.21037/gs-21-64).

Methods

A systematic literature search was performed in PubMed, Cochrane Library, and Scopus to identify and analyze studies published from November 2011 to September 2020 concerning robotic pancreatic surgery. The following terms were used to perform the search: "long term morbidity robotic pancreatic surgery".

The language of full-text articles was limited to English. All titles and abstracts were analyzed to select those concerning the long term morbidity of robotic pancreatic surgery. The research leads to 40 articles from PubMed, 32 from Scopus, and only one from Cochrane Library. 11 articles were excluded, matching PubMed results with Scopus because they were identical. Also, we excluded 26 studies on different topics or inappropriate. Some discussed only the laparoscopic approach. At last, we excluded meta-analysis, review, and book reports. Finally, we collect for our study 18 results (*Figures 1,2*).

Results

Eighteen articles included in the study were published between November 2011 and September 2020 (*Table 1*). The review included 2041 patients who underwent robotic pancreatic surgery, mainly for a malignant tumour. The two most common robotic surgical procedures adopted were the robotic distal pancreatectomy RDP (6-10) and the robotic pancreaticoduodenectomy (RPD) (2,3,11-13). In two studies (13,14)' patients were divided into groups, on the one hand, those who underwent a robotic pancreaticoduodenectomy (RPD), on the other hand, those who underwent robotic distal pancreatectomy (RDP). The remaining items included surgical approaches such as robotic middle pancreatectomy (RMP) (15,16), robotic distal pancreatectomy and splenectomy (17), robotic-assisted laparoscopic pancreatic dissection (RALPD) (18), robotic enucleation of pancreatic neuroendocrine tumors (19). At last, one study (20) evaluated outcomes of patients treated with modified robotic-assisted duodenum preserving pancreatic head resection (RA-DPPHR) and those treated with robotic-assisted pancreatoduodenectomy (RA-PD). All studies reported the median operative time (O.T.), except for Nassour *et al.* (14). The mean operative time ranged between 118 and 1,089 min; the O.T. was higher for robotic pancreatoduodenectomy than for distal pancreatectomy (PD 340–560 *vs.* DP 221–270 min). In a study (18) analyzing the learning curve of RLPD was reported a decreasing operative time from 2010 to 2013 (445 *vs.* 340 min). Blood loss was reported in 15 studies (3,6-8,10-13,15-21), with a range of 30–4,500 mL, more elevated for P.D. than for D.P. The case reported by Zhang *et al.* (15) concerning the use of RAMP in an elderly did not need blood transfusions. The conversion rate was analyzed in 12 studies (3,6,7,9-12,14,16,17,21). The overall conversion rate from the robotic approach to laparotomy varied between 0% to 18.2%, with rates higher in RPD than in laparoscopic pancreatoduodenectomy (OPD). Marino *et al.* (13) reported five conversions to open surgery (1 in D.P. and 4 in P.D.) for portal or superior mesenteric vein involvement, failure to progress with a high risk of inadequate oncologic resection, severe pancreatitis with massive disruption of pancreatic parenchyma on robotic touch and significant bleeding from the splenic artery (13). Massive bleeding was

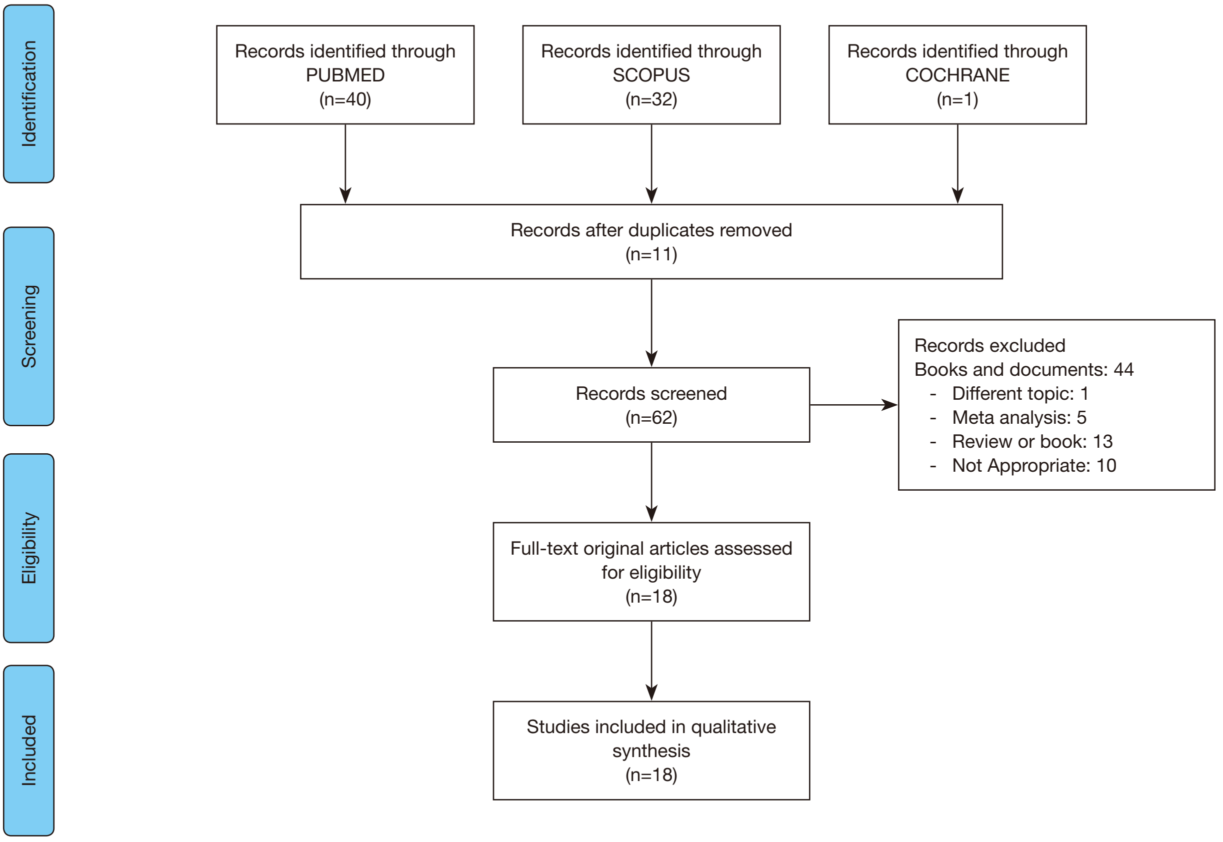

Figure 1 A PRISMA flow diagram.

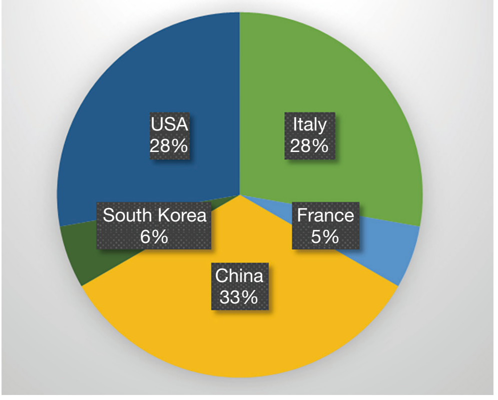

Figure 2 Regional distribution of the studies considered in this systematic review

described in the case of Yusheng *et al.* (16), where five patients (5%) underwent digital subtraction angiography, and four (4%) underwent reoperation to stop the bleeding (16). All the articles reported less hospital stay than open surgery, with a range of 0 and 58 days. Nassour *et al.* (14) demonstrated a decreased hospital stay associated with robotic pancreatic surgery compared to the open approach, with a 20% and 50% reduction in risk of prolonged length of stay for RPD and RDP, respectively (14).

Postoperative pancreatic fistula (POPF), based on the International Study Group for Pancreatic Fistula (ISGPF), represents one of D.P's most frequent complications. Except for Nassour *et al.* (14), all the authors reported the rate of POPF B and C with a variable range of 0% and 41.2%. In line with literature values, POPF rates were higher in patients treated with RPD than those who underwent RDP. Although the high value of POPF showed by Jiang *et al.* (20), in their review, there were no significant differences between RA-DPPHR and RA-PD groups in terms of frequencies of POPFs and biliary fistula (11.8% *vs.* 8.8%) (20). Postoperative complications were analyzed almost in all the reports through the Clavien-Dindo scoring system (CDC). The most important postoperative complication, besides POPF, were: wound infection, delayed gastric emptying, hemorrhagic

Table 1 Characteristics of the studies enrolled

Study	Year	Country	Design	Study interval	Setting	Robotic platform	Surgery procedures
Bencini *et al.* (2)	2019	Italy	Prospective study	January 2014 to December 2018	Single center	Da Vinci Si and Xi	RPD
Kim *et al.* (3)	2019	USA	Case study	–	Single center	–	RPD
Alfieri *et al.* (6)	2019	Italy	Comparative study	December 2008 to December 2016	Multicenter	Da Vinci Si and Xi platform	RDP: 53%
Benizri *et al.* (7)	2013	France	Prospective study	February 2004 to December 2011	Single center	–	RDPS: 54.5%, RDP: 45.5%
Lai *et al.* (8)	2015	China	Retrospective study	July 1999 to January 2015	Single center	Da Vinci Si	RDP: 47.1%, RDPS: 52.9%
Xourafas *et al.* (9)	2017	USA	Retrospective study	January 2014 to December 2014	Multicenter	–	RDP
Marino *et al.* (10)	2019	Italy	Case matched comparison	August 2014 to April 2016	Single center	Da Vinci Si	RPD
Zhang *et al.* (11)	2019	USA	Systematic review and meta-analysis	2000 to 2016	Multicenter	–	MIDP
Zureikat *et al.* (12)	2016	USA	Retrospective study	August 2011 to January 2015	Multicenter	–	RPD
Marino *et al.* (13)	2018	Italy	Retrospective analysis	January 2012 to July 2015	Single center	Da Vinci Si platform	RPD: 52%, RDP: 48%
Nassour *et al.* (14)	2020	USA (Pittsburgh)	Retrospective study	2010 to 2016	Single center	Da Vinci Si	RPD: 4%, RDP: 12%
Zhang *et al.* (15)	2015	China	Retrospective study	August 2012 to May 2015	Single center	–	RMP
Yusheng *et al.* (16)	2019	China	Retrospective study	August 2010 to July 2017	Single center	Da Vinci Si	RMP
Qu *et al.* (17)	2018	China	Retrospective study	December 2011 to December 2015	Sigle center	Da Vinci Si	RDPS
Chen *et al.* (18)	2015	China	Prospective study	January 2010 to December 2013	Single center	Da Vinci Si	RLPD
Di Benedetto *et al.* (19)	2018	Italy	Retrospective study	2013 to 2016	Multicenter study	Da Vinci Si and Xi	Robotic enucleation
Jiang *et al.* (20)	2017	China	Retrospective study	January 2010 to December 2016	Single center	Da Vinci Si	RA-DPPHR: 50%, RA-PD: 50%
Park *et al.* (21)	2019	South Korea	Retrospective study	October 2015 to October 2018	Multicenter	–	RDP

RA-DPPHR, duodenum preserving pancreatic head resection; RA-DP, robotic-assisted pancreaticoduodenectomy; RDP, robotic distal pancreatectomy; RDPS, robotic distal pancreatectomy and splenectomy; RAMP, robotic-assisted middle pancreatectomy; RPD, robotic pancreatoduodenectomy; RLPD, robotic-assisted laparoscopic pancreatoduodenectomy.

lesions, bile leakage (22). Because the most robotic pancreatic resections were performed for malignant diseases, almost all the studies (3,6,10,12-14,16-19,21,22) reported the rate of R0 resection. The oncological safety of the robotic approach in pancreatic surgery is not yet clear because long term follow-up and data about that are not available. Many studies figured out a rate of 100 % of R0 resection, in line with the literature. In contrast with these data, Zureikat *et al.* (12) reported a higher rate of microscopically positive surgical margins and a greater lymph node harvesting for RPD as compared with OPD. The multivariate analysis took in evidence that the operative approach was not independently associated with positive resection margin or tumor under staging (12). Ten articles (2,6-9,13,17,18,20,21) reported data relating to morbidity and 14 (2,6,8-10,12-14,16-18,20,22) about incidence of mortality. Nassour *et al.* (14) and Marino *et al.* (10) reported a reduction of the overall postoperative mortality rate in the robotic groups compared to the open one (10,14). In Marino *et al.*'s report, the median overall survival was nearly 35.3 months for RDP and 24.9 months for ODP. The analysis showed that intending to evaluate patients' safety and outcome underwent robotic pancreatic surgery, a reoperation rate of 6%, and 30-day postoperative mortality of 4%. The study evidenced a rate of R0 resection for patients treated with P.D. of 90.5% and 86.7% for the D.P. With a morbidity rate of 30% and a pancreatic fistula rate of 16%, and they did not found any differences between robotic and open surgery (13). Qu *et al.* (17) in the score-matched study described a median Overall Survival (O.S.) rate and a median disease-free survival (DFS) of 27 and 16 months, respectively for patients treated with RDP, demonstrating, besides, a similar result for the LDP group (17). In order to identify strong indicators of morbidity after DP, Xourafas *et al.* (9) found those in a higher Body max index (BMI >25), preoperative system sepsis, a preoperative hematocrit of less than 35%, the use of drains, and contaminated wound presence. Short-term postoperative morbidity was significantly lower when a vascular resection was not required or when patients were discharged to rehabilitation. Patients older than 62 years old, those who did not require a pancreatic reconstruction, those with a length of stay of more than 5 days and those discharged to rehabilitation had a odds of death within 30 days significantly reduced (9). As the morbidity rate so the mortality was lower than open surgery, the range was of 1–4% at 30 day and of 0–1.9% a 90 day. Benizri *et al.* (7) evaluated an overall morbidity rate of 50% in patients underwent robotic and laparoscopic distal pancreatectomy and a mortality rate of 0%. No significant differences were found between the two groups (7) (*Tables 2-5*).

Discussion

Pancreatic cancer is the fourth most common cause of adult cancer-related death, with 10.9–11.8 new cases per year (23). According to the National Cancer Institute (NCI), the mortality rates for pancreatic cancer in the USA is the same in the last two decades (24). Pancreatic resection was introduced between the 19th and 20th centuries by surgical innovators such as Billroth and Codivilla (25). With the development of advanced technology, minimally invasive techniques have increasingly been used in pancreatic surgery. Several studies reported that minimally invasive surgery improved perioperative pain control and led to postoperative morbidity rates and shorter postoperative hospital stay (26). However, laparoscopic surgery has limitations such as the restricted range of motion and two-dimensional vision; these restrictions could be overcome by robotic surgery. The Da Vinci robotic platform (Intuitive Surgical, Sunnyvale, CA, USA) provides a three-dimensional magnification of the camera system, articulated instrumentation, and increased freedom of movement for the surgical instruments (21). Da Vinci Si platform is an older system comparing with the Xi one; its main advantage is the use of a larger (12 mm) robotic camera with improved definition over the 8 mm camera (e.g., Xi) (3). The different configuration of the robot, with the Xi platform, reduces conflicts between the arms. Besides the possibility of switching the camera from a trocar to another, the table-motion feature makes it possible to change the configuration of the arms during the procedure.

On the contrary, the Si platform has only one arm dedicated to the camera, which does not allow the table's movement when it is docked to the patient. Another advantage of the Xi platform is the ability to approach larger surgical fields than the Si one (19). Since surgical system development, many reports have been published concerning minimally invasive robotic-assisted pancreatic surgery (5). With the growing expansion of robotic surgery, Melvin (27) and Giulianotti (28) described the first robotic distal pancreatectomy and pancreaticoduodenectomy, despite though the wide acceptance of this approach for pancreatic surgery is still low.

On the one hand, in the literature, several studies demonstrated that the robotic approach reduced the length of postoperative stay, giving a lower intraoperative blood loss, overall complication rate, and R0 resection margin rate

Table 2 Perioperative characteristics of the patients of the studies

Authors	Approach	Age	Male gender (%)	ASA score ≥ III	Malignant histologic subtype, n (%)	Anastomotic technique
Bencini *et al.* (2)	RPD	60 (42–73)	57.9%	15.8%	84.2%	PG 5.3%, Whipple 55.2%
	OPD	74 (56–91)	53%	36.1%	76%	
Kim *et al.* (3)	RPD	42	0%	–	100%	PG, HJ, Gj
	RDP	36.5%	47.9%	25%	42.7%	
Alfieri *et al.* (6)	LDP	27.1%	50.5%	21.2%	44.7%	Warshaw technique: 65.3%
Benizri *et al.* (7)	RDP	50.1	27.3%	9.1%	8.8%	–
	LDP	52.3	43.5%	13%		
Lai *et al.* (8)	RDP	61.2	58.8%	0%	23.5%	–
	LDP	63.2	22.2%		11.1%	
Xourafas *et al.* (9)	RDP	62 (22–88)	41%	67.5%	54%	–
	ODP	61 (18–88)	44%	70.3%	54%	–
	LDP	62 (19–89)	40%	64.3%	52%	–
Marino *et al.* (10)	RPD	60.4 (43–72)	54.3%	20%	82.9%	PJ
	OPD	62.3 (45–73)	42.9%	22%	77.2%	
Zhang *et al.* (11)	MIDP	59 (50–66)	43.5%	–	26.6%	Spleen preserving 24.3%
	ODP	56 (47–65)	46.7%	–	26%	
Zureikat *et al.* (12)	RPD	67 (15–86)	55.45%	–	33.2%	–
	OPD	65 (15–93)	52.3%	–	55.3%	
Marino *et al.* (13)	RDP	62 (35–79)	60%	22%	30%	PJ
	RPD				42%	
Nassour *et al.* (14)	RDP	67	44%	–	26%	–
	ODP	66	47%		28%	
	RPD	67	50%	–	27%	
	OPD	66	52%		33%	
Zhang *et al.* (15)	RMP	64.3	70%	–	0%	PG
Yusheng *et al.* (16)	RMP	46.4–49	31%	7.4%	–	PG
Qu *et al.* (17)	RDP	59.9	46.5%	2.3%	88.6%	–
	LDP	57.8	65.8%	2.6%	88.6%	
Chen *et al.* (18)	RPD	53.6	57%	1.7%	63.3%	PG, HJ, GJ
	OPD	53.8	54.2%	1.6%	63.3%	
Di Benedetto *et al.* (19)	RE	53.8	50%	17%	25%	–
Jiang *et al.* (20)	RDP	47	23.5%	52.9%	0%	PG, PJ
	RPD	47.4	38.2%	41.2%		
Park *et al.* (21)	RDP	47.3 (21–74)	19.2%	7.7%	3.8%	Spleen preserving 34.6%

ASA score, American Society of Anaesthesiologists physical status classification system; RDP, robotic distal pancreatectomy; RPD, robotic pancreaticoduodenectomy; OPD, open pancreatoduodenectomy; ODP, open distal pancreatectomy; LDP, laparoscopic distal pancreatectomy; LPD, laparoscopic pancreaticoduodenectomy; MIDP, minimal invasive distal pancreatectomy; RMP, robotic middle pancreatectomy; P.J., pancreaticojejunostomy; P.G., pancreaticogastrostomy; H.J., hepaticojejunostomy.

Table 3 Operative characteristics, mortality and morbidity of patients undergoing Robotic pancreatic surgery versus open pancreatic surgery

Authors, year	Approach	N	LOH	Op-Time	EBL	Conv. rate	R0	Clavien ≥ III	Mortality (30 days)	Morbidity
Bencini *et al.* (2)	RPD	38	8	545	–	–	–	55.3%	2.9%	52.6%
	OPD	83	10	351	–	–	–	54%	3.3%	50%
Xourafas *et al.* (9)	RDP	200	5	243	–	8%	–	–	0.5%	37%
	ODP	921	7	222	–	–	–	–	1.5%	–
Marino *et al.* (10)	RPD	35	6.5	355	235	8.6%	94%	31.4%	2.9%	–
	OPD	35	8.9	262	575	–	77%	48.6%	2.9%	–
Zhang *et al.* (11)	RDP	214	5	210	100	–	–	92%	–	48.2%
	ODP	362	7	210	300	–	–	83%	–	58.25
	RPD	211	8	402	200	–	50%	23.7%	1.9%	–
Zureikat *et al.* (12)	OPD	817	8	300	300		69%	23.85%	2.82%	–
	RDP	332	6	–	–	12%	84.6%	–	0.3%	–
Nassour *et al.* (14)	ODP	2,386	8	–	–	–	23.2%	–	2%	–
	RPD	626	10	–	–	15%	76.8%	–	2%	–
	OPD	17,205	11	–	–	–	78.2%	–	3%	–
Chen *et al.* (18)	RPD	60	20	393	350	–	–	11.7%	1.7%	35%
	OPD	120	25	323	500	–	–	13.3%	2.5%	40%

R0, tumour free margins; RDP, robotic distal pancreatectomy; RPD, robotic pancreaticoduodenectomy; OPD, open pancreatoduodenectomy; ODP, open distal pancreatectomy; LDP, laparoscopic distal pancreatectomy; LPD, laparoscopic pancreaticoduodenectomy; MIDP, minimal invasive distal pancreatectomy; RMP, robotic middle pancreatectomy; P.J., pancreaticojejunostomy; P.G., pancreaticogastrostomy; H.J., hepaticojejunostomy; LOH, length of hospitalization; EBL, estimated blood loss.

Table 4 Operative characteristics, mortality and morbidity of patients undergoing robotic pancreatic surgery versus laparoscopic pancreatic surgery

Authors, year	Approach	N	LOH	Op-Time	EBL	Conv. rate	R0	Clavien ≥ III	Mortality (30 days)	Morbidity
Alfieri *et al.* (6)	RDP	96	11	270.02	162.5	9.4%	100%	11.2%	1%	46.9%
	LDP	85	10	233.7	233.7	14.1%	98.8%	10.5%	0%	44.7%
Benizri *et al.* (7)	RDP	11	10	225	515	18.2%	–	27.3%	1%	50%
	LDP	23	9	194	345	21.7%	–	17.4%	0%	33%
Lai *et al.* (8)	RDP	17	11.4	221.4	100.3	–	–	65%	0%	47.1%
	LDP	18	14.2	173.6	268.3	–	–	55%	0%	38.9%
Xourafas *et al.* (9)	RDP	200	5	243	–	8%	–	–	0.5%	–
	LDP	694	5	205	–	9%	–	–	1%	–
Qu *et al.* (17)	RDP	35	9.2	223.3	100	5.7%	100%	5.7%	0%	37.1%
	LDP	35	8.6	207.2	200	23%	97.1%	8.6%	0%	40%

Table 5 Operative characteristics, mortality and morbidity of patients who underwent robotic surgery

Authors, year	Approach	N	LOH	Op-Time	EBL	Conv. rate	R0	Clavien ≥ III	Mortality (30 days)	Morbidity
Kim *et al.* (3)	RPD	1	6	225	50	0%	100%	0%	–	–
Marino *et al.* (13)	RDP	24	8	260	100	4.2%	86.7%	20.8%	4.2%	–
	RPD	26	13	540	290	15.3%	90.5%	38.5%	3.8%	–
Zhang *et al.* (15)	RMP	10	19.91	175	0	–	–	30%	0%	30%
Yusheng *et al.* (16)	RMP	100	24.8	158.9	84.3	0%	100%	22%	1%	–
Di Benedetto *et al.* (19)	RDP	12	3.9	203.17	38.3	0%	100%	33.3%	0%	–
Jiang *et al.* (20)	RDP	34	20.1	188.3	168.2	–	–	11.8%	–	47%
	RPD	34	23.9	386.3	409.4	–	–	14.7%	–	32.4%
Park *et al.* (21)	RDP	26	7	173	50	1%	100%	25.9%	–	3.8%

similar to open surgery. On the other hand, robotic surgery still presents drawbacks regarding its high costs and unclear oncological results (13). Alfieri *et al.* showed a recurrence rate, after RADP, of 6.9% in a mean time of 23.4 months represented by pulmonary metastases and hepatic metastases. In contrast, reports like the one of Boggi *et al.* (29) and Lai *et al.* (8) found less positive margin in the minimally invasive group than in the open approach (8,29). Positive margin and lymph nodes (LN) harvested are two important malignancy prognosis factors for pancreatic cancer, and the ability of surgeons could influence them. According to this hypothesis, Zhang *et al.* (22) analyzed the R0 resection rate and the number of lymph nodes harvested in the first 40 patients who underwent RPD compared to the later 60 patients who underwent the same operation. The results suggested a similar R0 resection rate, a similar rate of postoperative complications but an increased rate of lymph nodes harvested (22). Adequate LN sampling is a significant cancer surgery component that provides an accurate staging and risk stratification. A multi-institutional study (12) confirmed the association between RPD and the increased number of harvested LNs, suggesting the advantages of these findings mainly around the superior mesenteric artery. At the same time, it is essential to add that a significant part of robotic cases in this analysis was performed at high-volume centres where high-volume surgeons and specialized pathologists may lead to higher LN yield (14). As demonstrated by several authors (13,30,31), the gentle and meticulous dissection around large vessels allows a high rate of spleen-preserving procedures. Also, 7 degrees of freedom instruments help obtain good oncologic adequacy reaching difficult anatomic zones as the celiac nerve plexus, which is often a recurrence site (13,30,31).

For many years only benign and low-grade malignant pancreatic tumors have been treated by laparoscopic surgery; however, recent studies suggest as laparoscopy could be feasible and effective in treating pancreatic cancer. The using of Yonsei Criteria (tumor confined to the pancreas, intact fascia layer between the distal pancreas and the left adrenal gland and kidney, and tumor located more than 1–2 cm from the celiac axis) for evaluating if treatment with laparoscopic radical distal pancreatectomy is indicated, makes minimally invasive techniques highly safe and effective for achieving bloodless and margin-negative resection during the treatment of left-sided pancreatic cancer. Furthermore, studies demonstrated more also favorable long-term oncologic outcomes for patients with tumor that meet all three criteria (32). NCCN guideline version 1. 2020 pancreatic adenocarcinoma recommended surgical treatment by laparotomy or minimally invasive surgery as a treatment for resectable pancreatic cancer. Considering the oncologic significance of retroperitoneal margin in treating pancreatic cancer, to secure them during LPD, Rho *et al.* (33) introduced the potential application of indocyanine green to facilitate the securement of the SMA (superior mesenteric artery) lateral margin in laparoscopic PD (33). With the same aim, Kuroki *et al.* (34) introduced the concept of the pancreas-hanging maneuver by Penrose drain in managing SMA margin during LDP (34).

For advanced pancreatic cancer, only a few case reports and case series have been reported on the technical feasibility and safety of LPD with combined venous vascular resection. Several authors (35,36) demonstrated no statistical significance between LPD and OPD in terms of overall survival. These studies confirmed that there was no significant difference in the 5-year overall survival. In addition, LPD resulted in a higher rate of R0 resection, more harvested lymph nodes, shorter hospital stays and less estimated blood loss, so LPD is not inferior to OPD respect to long term oncologic outcomes as well as better short term surgical outcomes in patients with pancreatic cancer (35,36). Sharpe *et al.* (37) showed that patients who underwent LPD for pancreatic cancer in high volume centers had equivalent outcomes than OPD patients concerning on length stay, R0 resection, lymph node count and readmission rate (37). Furthermore, Kantor *et al.* (38) found comparable short term and long-term overall survival outcomes with OPD and LPD (38). On the basis of the last study recently performed by Van Hilst *et al.* (39) nine surgeons demonstrated the safety concerns with LPD. They recognized that technical feasibility, procedural safety and surgical extent for margin negative resection should be considered in defining potential indication of LPD (36,39). According to the literature, LPD could be a good alternative strategy in managing well-selected resectable pancreatic cancer.

In addition, concerning the oncological safety of the robotic technique, in literature, some studies confirm the reduction of hospital stay of robotic more than laparoscopy and open. This characteristic and its potential benefit with a less immunological response and faster adjuvant chemotherapy could lead to better survival (29). Besides, Anderson *et al.* (40) demonstrated that patients who underwent minimally invasive distal pancreatectomy were more likely to receive adjuvant chemotherapy, which may explain the survival difference (40).

An important factor affecting the robotic approach is the operative time. Alfieri *et al.* (6) found a more prolonged operative time for RDP than LDP due to the docking time and the learning curve. On the one hand, the robotic set-up took a meantime, representing 8% of all the procedure duration; on the other hand, the surgeon's progressive experience in this new technique led to a reduction of the operative duration. Also, the propensity to use the Warshaw technique (splenic preservation during a distal pancreatectomy performed with splenic vessel ligation), for its complexity, leads to more prolonged operative time (6,41). The robotic approach seems to improve haemorrhage control better than the laparoscopic approach; thanks to using a 3D vision and the rapid switch from monopolar to bipolar energy, surgeons could control bleeding. Simultaneously, the capability to perform hand-sewn ligation during gastroduodenal artery control provides a low risk of postoperative pseudoaneurysm (13,42,43). Chen *et al.* (18) demonstrated that blood loss from RLPD decreased during the "learning curve", and the large degree of freedom enables the surgeons to complete complex vessel reconstruction. They suggested that venous involvement may not be an absolute contraindication to robotic surgery; prosthetic graft reconstruction can be completed using the robotic surgery approach. Even if the robotic approach seems to improve different aspects of pancreatic surgery, the occurrence and severity of POPF did not reduce with robotic assistance (18).

The surgical technique results in a significant reduction of postoperative complications and improving patient's quality of life. Hence, Beger (44) in 1972 described the duodenum-preserving pancreatic head resection (DPPHR) for patients with severe pancreatitis to preserve the digestive tract's integrity while cutting off the head of the pancreas. Since that, DPPHR has become an effective surgical option for benign and premalignant pancreatic head lesions (44). Jiang *et al.* (20) analyzing the short and long-term outcomes of modified RA-DPPHR and RA-PD (robotic-assisted pancreatoduodenectomy), did not observe P.G. (pancreaticogastrostomy) fistulas. It suggested that the orig]in of pancreatic leakage could be from the proximal pancreatic stump rather than from the P.G.

Another great aspect of the surgery technique useful for avoiding the incidence of exocrine and endocrine insufficiency is that the use of a pancreaticogastrostomy could preserve the digestive tract's continuity and integrity. It is easier to perform a P.G. in robotic-assisted operations, such as in open technique, thanks to the short distance between pancreatic stumps and the stomach's posterior wall (45). It seems that P.G. led to a lower cumulative incidence of exocrine failure but a similar incidence of endocrine insufficiency and pancreatic fistula (46). Besides, as a complication, afferent loop obstruction was statistically frequent in the robotic approach, more than in OPD. It occurs in 0.3% of patients undergoing gastroenterostomy due to intestinal adhesion and angulation, internal hernia, anastomotic structure, and tumor recurrence (47,48).

In light of the propensity of pancreatic cancer to be metastatic at the time of the diagnosis, adjuvant chemotherapy could improve morbidity and substantially affect survival. Trials demonstrated an improved 10-year overall and disease-free survival rates with adjuvant gemcitabine in resected patients. The morbidity associated with pancreatic resection has a role in the ability of patients to receive adjuvant treatment. Complications are associated with a delay in the initiation of adjuvant treatment. Also, it seems that patients without postoperative complications had a significantly longer median survival than those with complications (19.5 *vs.* 16.1) (49). In high volume centres, the minimally invasive pancreatic resections demonstrate the potential benefit of minimizing the morbidities that hinder patient access to adjuvant therapy (50). Lee *et al.* (51) reported a significant survival benefit of mini-invasive surgery compared to the open group for disease-free and overall survival. Besides, patients without lymph node metastasis had a 5-year survival rate of 77.8%, suggesting a role of this group in the category of early pancreatic cancer (51). Nassour *et al.* (14) found no difference in 30 and 90-day mortality between RPD and OPD. On the contrary, the robotic approach was associated with lower postoperative mortality. The most significant finding of this analysis was the superior long-term survival associated with the use of the robotic platform for R.D. (14), the same results that Sulpice *et al.* (52) found comparing LDP to ODP (52). Quality of life (QOL) for pancreatic cancer is a crucial studied metric. Some studies demonstrated that pancreatic cancer patients undergoing resection are less likely to enrol in hospice and more likely to receive aggressive care at the end of life, so the intensity of care in the final month of life has increased in the last years (53). Also, RLPD patients presented a significantly faster nutritional status recovery thanks to the earlier resumption of oral intake, less incisional pain, and more relaxed psychological status (54).

Robotic surgery also allows some integrations, such as using U.S. scan and FireFly fluorescence technology to provide a precise localize of the lesion, the main pancreatic duct, and the vessels overcoming the absence of tactile sense and avoiding surgical injuries (19).

Conclusions

Comparison between robotic surgery and open surgery lead to evidence of different advantages of the robotic approach. A multidisciplinary team and a surgical center at high volume are essential for better postoperative morbidity and mortality. It is still doubtful if oncological results and cost-effectiveness are really adequate for the use of robotic pancreatic surgery. The robotic platform may contribute to additional costs regarding one procedure. However, it is the overall cost reduction of performing a wide range of procedures in a minimally invasive way that must be evaluated. As an expensive investment, the overall cost-effectiveness should be calculated on the total number of cost reductions deriving from all robotic-assisted procedures that would have been otherwise performed open or laparoscopically. Other aspects that are often overlooked concerning the advantages of minimally invasive surgery in the long term. Furthermore, the robotic platform will eventually become more affordable over time, especially when competitors share the market, which is currently a monopoly. Pancreatic surgery represents one of the most successful fields of applying the robotic platform, and its use is growing at an astonishing pace.

Like a randomized clinical trial, further research is necessary to confirm the evidence reported in this review.

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Footnote

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References

1. Kornaropoulos M, Moris D, Beal EW, et al. Total robotic

pancreaticoduodenectomy: a systematic review of the literature. Surg Endosc 2017;31:4382-92.
2. Bencini L, Annecchiarico M, Farsi M, et al. Minimally invasive surgical approach to pancreatic malignancies. World J Gastrointest Oncol 2015;7:411.
3. Kim AC, Rist RC, Zureikat AH. Technical Detail for Robot Assisted Pancreaticoduodenectomy. J Vis Exp 2019;(151). doi: 10.3791/60261.
4. Li J, Wientjes MG, Au JL. Pancreatic Cancer: Pathobiology, Treatment Options, and Drug Delivery. AAPS J 2010;12:223-32.
5. Fernandes E, Giulianotti PC. Robotic-assisted pancreatic surgery. J Hepatobiliary Pancreat Sci 2013;20:583-9
6. The Italian Robotic pNET Group, Alfieri S, Butturini G, et al. Short-term and long-term outcomes after robot-assisted versus laparoscopic distal pancreatectomy for pancreatic neuroendocrine tumors (pNETs): a multicenter comparative study. Langenbecks Arch Surg 2019;404:459-68.
7. Benizri EI, Germain A, Ayav A, et al. Short-term perioperative outcomes after robot-assisted and laparoscopic distal pancreatectomy. J Robot Surg 2014;8:125-32.
8. Lai ECH, Tang CN. Robotic distal pancreatectomy versus conventional laparoscopic distal pancreatectomy: a comparative study for short-term outcomes. Front Med 2015;9:356-60.
9. Xourafas D, Ashley SW, Clancy TE. Comparison of Perioperative Outcomes between Open, Laparoscopic, and Robotic Distal Pancreatectomy: an Analysis of 1815 Patients from the ACS-NSQIP Procedure-Targeted Pancreatectomy Database. J Gastrointest Surg 2017;21:1442-52.
10. Marino MV, Podda M, Gomez Ruiz M, et al. Robotic-assisted versus open pancreaticoduodenectomy: the results of a case-matched comparison. J Robot Surg 2020;14:493-502.
11. Zhang XF, Lopez-Aguiar AG, Poultsides G, et al. Minimally invasive versus open distal pancreatectomy for pancreatic neuroendocrine tumors: An analysis from the U.S. neuroendocrine tumor study group. J Surg Oncol 2019;120:231-40.
12. Zureikat AH, Postlewait LM, Liu Y, et al. A Multi-institutional Comparison of Perioperative Outcomes of Robotic and Open Pancreaticoduodenectomy: Ann Surg 2016;264:640-9.
13. Marino MV, Shabat G, Potapov O, et al. Robotic pancreatic surgery: old concerns, new perspectives. Acta Chir Belg 2019;119:16-23.
14. Nassour I, Winters SB, Hoehn R, et al. Long-term oncologic outcomes of robotic and open pancreatectomy in a national cohort of pancreatic adenocarcinoma. J Surg Oncol 2020;122:234-42
15. Zhang T, Wang X, Huo Z, et al. Robot-Assisted Middle Pancreatectomy for Elderly Patients: Our Initial Experience. Med Sci Monit 2015;21:2851-60.
16. Shi Y, Wang Y, Wang J, et al. Learning curve of robot-assisted middle pancreatectomy (RMP): experience of the first 100 cases from a high-volume pancreatic center in China. Surg Endosc 2020;34:3513-20.
17. Qu L, Zhiming Z, Xianglong T, et al. Short- and mid-term outcomes of robotic versus laparoscopic distal pancreatosplenectomy for pancreatic ductal adenocarcinoma: A retrospective propensity score-matched study. Int J Surg 2018;55:81-6.
18. Chen S, Chen JZ, Zhan Q, et al. Robot-assisted laparoscopic versus open pancreaticoduodenectomy: a prospective, matched, mid-term follow-up study. Surg Endosc 2015;29:3698-711.
19. Di Benedetto F, Magistri P, Ballarin R, et al. Ultrasound-Guided Robotic Enucleation of Pancreatic Neuroendocrine Tumors. Surg Innov 2019;26:37-45.
20. Jiang Y, Jin JB, Zhan Q, et al. Robot-assisted duodenum-preserving pancreatic head resection with pancreaticogastrostomy for benign or premalignant pancreatic head lesions: a single-centre experience. Int J Med Robot 2018;14:e1903.
21. Park G, Choi SH, Lee JH, et al. Safety and Feasibility of Robotic Reduced-Port Distal Pancreatectomy: a Multicenter Experience of a Novel Technique. J Gastrointest Surg 2020;24:2015-20.
22. Zhang T, Zhao ZM, Gao YX, et al.The learning curve for a surgeon in robot-assisted laparoscopic pancreaticoduodenectomy: a retrospective study in a high-volume pancreatic center. Surg Endosc 2019;33:2927-33.
23. Jemal A, Siegel R, Ward E, et al. Cancer Statistics, 2006. CA Cancer J Clin 2006;56:106-30.
24. StatBite U.S. Pancreatic Cancer Rates | JNCI: Journal of the National Cancer Institute | Oxford Academic.
25. Schnelldorfer T, Adams DB, Warshaw AL, et al. Forgotten pioneers of pancreatic surgery: beyond the favorite few. Ann Surg 2008;247:191-202.
26. Tan HL, Tan EK, Teo JY, et al. Outcome of minimally-invasive versus open pancreatectomies for solid pseudopapillary neoplasms of the pancreas: A 2:1 matched case-control study. Ann Hepatobiliary Pancreat Surg

2019;23:252.
27. Melvin WS, Needleman BJ, Krause KR, et al. Robotic resection of pancreatic neuroendocrine tumor. J Laparoendosc Adv Surg Tech A 2003;13:33-6.
28. Giulianotti PC, Coratti A, Angelini M, et al. Robotics in general surgery: personal experience in a large community hospital. Arch Surg Chic Ill 1960 2003;138:777-84.
29. Boggi U, Napoli N, Costa F, et al. Robotic-Assisted Pancreatic Resections. World J Surg 2016;40:2497-506.
30. Shakir M, Boone BA, Polanco PM, et al. The learning curve for robotic distal pancreatectomy: an analysis of outcomes of the first 100 consecutive cases at a high-volume pancreatic centre. HPB 2015;17:580-6.
31. Hwang HK, Kang CM, Chung YE, et al. Robot-assisted spleen-preserving distal pancreatectomy: a single surgeon's experiences and proposal of clinical application. Surg Endosc 2013;27:774-81.
32. Chong JU, Kim SH, Hwang HK, et al. Yonsei criteria: a clinical reflection of stage I left-sided pancreatic cancer. Oncotarget 2017;8:110830-6.
33. Rho SY, Kim JS, Chong JU, et al. Indocyanine Green Perfusion Imaging-Guided Laparoscopic Pancreaticoduodenectomy: Potential Application in Retroperitoneal Margin Dissection. J Gastrointest Surg 2018;22:1470-4.
34. Kuroki T, Tajima Y, Kitasato A, et al. Pancreas-hanging maneuver in laparoscopic pancreaticoduodenectomy: a new technique for the safe resection of the pancreas head. Surg Endosc 2010;24:1781-3.
35. Croome KP, Farnell MB, Que FG, et al. Pancreaticoduodenectomy with Major Vascular Resection: a Comparison of Laparoscopic Versus Open Approaches. J Gastrointest Surg 2015;19:189-94.
36. Kang CM, Lee WJ Is Laparoscopic Pancreaticoduodenectomy Feasible for Pancreatic Ductal Adenocarcinoma? Cancers 2020;12:3430.
37. Sharpe SM, Talamonti MS, Wang CE, et al. Early National Experience with Laparoscopic Pancreaticoduodenectomy for Ductal Adenocarcinoma: A Comparison of Laparoscopic Pancreaticoduodenectomy and Open Pancreaticoduodenectomy from the National Cancer Data Base. J Am Coll Surg 2015;221:175-84.
38. Kantor O, Talamonti MS, Sharpe S, et al. Laparoscopic pancreaticoduodenectomy for adenocarcinoma provides short-term oncologic outcomes and long-term overall survival rates similar to those for open pancreaticoduodenectomy. Am J Surg 2017;213:512-5.
39. Van Hilst J, de Rooij T, Bosscha K, et al. Laparoscopic versus open pancreatoduodenectomy for pancreatic or periampullary tumours (LEOPARD-2): a multicentre, patient-blinded, randomised controlled phase 2/3 trial. Lancet Gastroenterol Hepatol 2019;4:199-207.
40. Anderson KL, Adam MA, Thomas S, et al. Impact of minimally invasive vs. open distal pancreatectomy on use of adjuvant chemoradiation for pancreatic adenocarcinoma. Am J Surg 2017;213:601-5.
41. Shoup M. The Value of Splenic Preservation With Distal Pancreatectomy. Arch Surg 2002;137:164.
42. Boggi U, Amorese G, Vistoli F, et al. Laparoscopic pancreaticoduodenectomy: a systematic literature review. Surg Endosc 2015;29:9-23.
43. Wright GP, Zureikat AH. Development of Minimally Invasive Pancreatic Surgery: an Evidence-Based Systematic Review of Laparoscopic Versus Robotic Approaches. J Gastrointest Surg 2016;20:1658-65.
44. Beger HG, Büchler M, Bittner RR, et al. Duodenum-Preserving Resection of the Head of the Pancreas in Severe Chronic Pancreatitis: Early and Late Results. Ann Surg 1989;209:273-8.
45. Serra F, Barbato G, Tazzioli G, et al. Pancreaticogastrostomy as reconstruction choice in pancreatic trauma surgery: Case report and review of the literature. Int J Surg Case Rep 2019;65:102-6.
46. Iacono C, Verlato G, Ruzzenente A, et al. Systematic review of central pancreatectomy and meta-analysis of central versus distal pancreatectomy. Br J Surg 2013;100:873-85.
47. Blachar A, Federle MP, Pealer KM, et al. Gastrointestinal complications of laparoscopic Roux-en-Y gastric bypass surgery: clinical and imaging findings. Radiology 2002;223:625-32.
48. Jordan GL Jr. Surgical management of postgastrectomy problems. Arch Surg 1971;102:251-9.
49. Wu W, He J, Cameron JL, et al. The impact of postoperative complications on the administration of adjuvant therapy following pancreaticoduodenectomy for adenocarcinoma. Ann Surg Oncol 2014;21:2873-81.
50. Maggi JC, Hogg ME, Zureikat AH, et al. Update on the Management of Pancreatic Cancer: Determinants for Surgery and Widening the Therapeutic Window of Surgical Resection. Curr Surg 2016;Rep 4:26.
51. Lee SH, Kang CM, Hwang HK, et al. Minimally invasive RAMPS in well-selected left-sided pancreatic cancer within Yonsei criteria: long-term (>median 3 years) oncologic outcomes. Surg Endosc 2014;28:2848-55.
52. Sulpice L, Farges O, Goutte N, et al. Laparoscopic Distal

Pancreatectomy for Pancreatic Ductal Adenocarcinoma: Time for a Randomized Controlled Trial? Results of an All-inclusive National Observational Study. Ann Surg 2015;262:868-73; discussion 873-4.
53. Bliss LA, Witkowski ER, Yang CJ, et al. Outcomes in operative management of pancreatic cancer: Outcomes in Operative Management of Pancreatic Cancer. J Surg Oncol 2014;110:592-8.
54. Fearon KCH, Ljungqvist O, Von Meyenfeldt M, et al. Enhanced recovery after surgery: a consensus review of clinical care for patients undergoing colonic resection. Clin Nutr 2005;24:466-77.

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