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Review

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Minimally invasive left pancreatectomy for pancreatic ductal adenocarcinoma: review of the current literature

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Abstract

The minimally invasive approach has gained popularity in the last decades, even in complex abdominal surgery such as pancreatic resections. Currently, many meta-analyses focus on the benefits and advantages of the minimally invasive approach compared to open surgery, especially during left pancreatectomy (LP). Limited data on the oncological outcomes are available. The review aims to describe the surgical and oncological outcomes of the minimally invasive left pancreatectomy (MILP). The search terms were based on the final histological pathology (pancreatic adenocarcinoma) and the comparison of different surgical approaches (open *vs.* minimally invasive). The search strategy was constructed in PubMed and adapted to run across other database platforms, focusing on studies published until 2022. A total of 2,878 studies were selected and duplicates were removed. After title and abstract screening, 109 articles remained for full-text assessment, of which 28 met the eligibility criteria for this systematic review. Considering the study design, the studies were divided into retrospective (n = 15), prospective (n = 4), and 13 propensity score-matched (n = 9). The present review of the literature suggests that MILP is technically feasible and safe for treating body and tail pancreatic ductal adenocarcinoma (PDAC). MILP did not have any impact on the major complications, reducing hospitalization. Regarding the oncological outcomes, the surgical technique did not have an impact on the R0 resection rate, lymph node harvested rate, use

of adjuvant chemotherapy, and overall survival. Further prospective randomized trials remain indicated to assess the oncological impact of the MILP in patients with PDAC.

Keywords: Pancreatic cancer, laparoscopic distal pancreatectomy, robotic distal pancreatectomy, pancreatic resection

INTRODUCTION

The minimally invasive approach to the left-side pancreatic lesions is, actually, considered safe, feasible, and quite easy in expert hands. However, no consensus and robust data in the literature are obtained regarding the use of the minimally invasive approach in the treatment of pancreatic cancer [pancreatic ductal adenocarcinoma (PDAC)]. Since the first report by Gagner in 1996[1], the laparoscopic approach to left pancreatectomy (LP) has gained popularity worldwide, becoming the gold-standard approach for benign and low-grade malignancy lesions of the pancreatic body-tail. The introduction of robotic platforms for performing LP in 2002 contributed to the widespread adoption of minimally invasive pancreatic surgery (MIPS)[2].

After an initial phase where the studies primarily focused on evaluating the safety and feasibility of MIPS on benign or pre-neoplastic lesions, the main effort of the scientific community forthwith changed to try to assess the adequacy and safety of the oncological treatment of PDAC[3]. Although the 2019 Miami guidelines encouraged adopting the minimally invasive approach for all left-side pancreatic lesions, skepticism persisted within the surgical community[4]. This skepticism was highlighted in two recent international surveys, where 19% to 31% of surgeons believed minimally invasive left pancreatectomy (MILP) to be inferior to open LP (OLP) in patients with PDAC[5,6].

Several studies comparing the MILP to OLP consider short-term or surgical outcomes. Few studies focused on the oncological results. However, most of them reported data about all the malignant pancreatic lesions without focusing on PDAC. A large Cochrane review tried to analyze the MILP series on PDAC. The report included 12 studies, demonstrating that different surgical techniques did not have any impact on oncological outcomes, such as tumor negative resection margins (R0), recurrence, and survival. However, all included studies were of very low quality[7].

Recently, data of the literature improved in quality due to the publication of large multicenter or propensity-matched cohort studies. This systematic review aims to compare the short-term and oncological outcomes of patients who underwent minimally invasive *vs.* open left pancreatic resections.

METHODS

This systematic review was conducted following the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines [Figure 1] and the Cochrane Handbook for Systematic Reviews of Interventions[8,9].

Literature search

The search terms were derived from the final histological pathology (PDAC) and a comparison of different surgical approaches (open *vs.* minimally invasive). The search strategy was designed in PubMed and adapted for Ovid and Web of Science databases, focusing on studies published until 2022. The PubMed research was as follows:

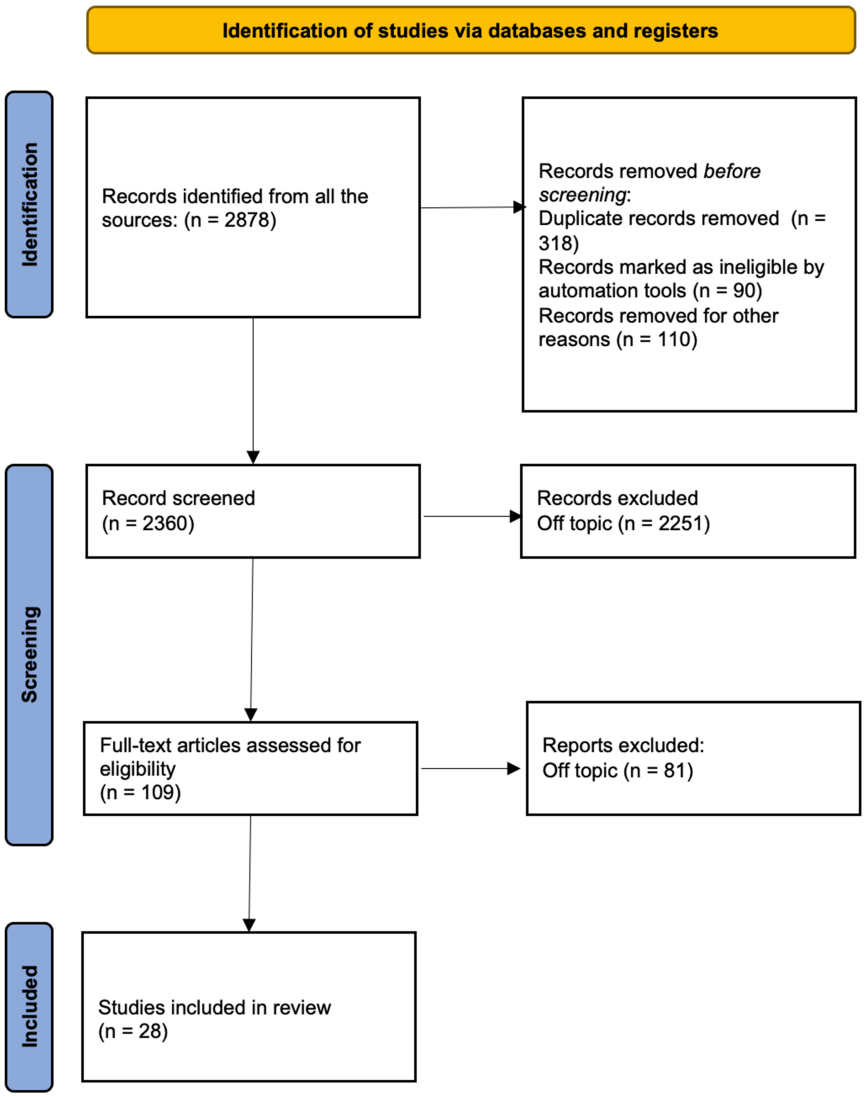

Figure 1. The PRISMA study selection flowchart. PRISMA: Preferred reporting items for systematic reviews and meta-analyses.

((((((“Pancreatic Neoplasms”[Mesh]) OR pancreatic adenocarcinom* [tiab]) OR malignan* [tiab]) OR tumo* [tiab])) AND (((((“Pancreatectomy”[Mesh]) OR distal pancreatectom* [tiab]) OR left pancreatectom* [tiab]) OR spleno pancreatectom* [tiab]) OR pancreatosplenectom* [tiab])) AND ((((“Laparoscopy”[Mesh]) OR laparoscop* [tiab]) OR robot* [tiab]) OR minimally invasive* [tiab]).

Eligibility criteria

Studies must report a comparison of different surgical approaches, such as minimally invasive surgery (laparoscopic or robotic) versus open surgery for the treatment of PDAC in the distal pancreas. Non-English studies, duplicates, editorials, animal studies, and studies involving children were excluded. If the outcomes of interest were not reported or indirectly inferable, the study was also excluded. Small case series (< 10 cases per surgical approach) were not selected for the review. Studies reporting data extracted from national or international databases were screened and only the most recent study was included.

Study selection

Two reviewers (MDP and AC) independently screened the research results based on titles and abstracts, followed by full-text evaluation for eligibility. The full-text eligibility selection was conducted independently by MDP and AC following the Scottish intercollegiate guidelines network (SIGN) methodology[10,11]. Any conflicts were resolved using discussion until a consensus was reached.

Risk of bias

Two independent reviewers (MDP and AC) assessed the study quality according to the Newcastle Ottawa Scale (NOS) for all studies since no randomized controlled trials (RCTs) were expected to be included. The NOS checklist consisted of three different quality parameters: comparability of groups, selected population, and assessment of either the exposure or outcome of interest for case-control or cohort studies. A final score was assigned to each study, ranging from 0 to 9. Studies with a score of 7 or higher were considered high-quality.

Inclusion criteria

The studies included must be written in English, report a study population of more than 20 patients who underwent LP for PDAC, and describe intra-, postoperative, and oncological parameters. To avoid data overlap, the most informative or recent article was considered if the data provided came from the same Institution's database.

Exclusion criteria

Abstracts, case series, no comparing analysis, review articles, partial or incomplete data reporting, case reports, animal studies, studies involving children, or non-English manuscripts were excluded from the systematic review.

Data extraction

Two different reviewers (MDP and AC) extracted data following a predefined evidence table. Data consisted of study design, study period, country, sample size, type of surgical approach, demographic information [age, body mass index (BMI), American Society of Anesthesiology (ASA) score, neoadjuvant therapy], intraoperative characteristics (operative time, estimated blood loss, vascular resection, multi-visceral resection, and conversion rate), postoperative outcomes (postoperative major complications classified by Clavien-Dindo[12], postoperative pancreatic fistula, post pancreatectomy hemorrhage, delayed gastric empty, and length of hospital stay), and oncological outcomes (R0 resection, harvested lymph nodes, adjuvant chemotherapy, and survival). All pancreas-specific complications were classified by the International Study Group of Pancreatic Surgery (ISGPS) definitions[13-15].

RESULTS

Search results

The literature research resulted in 2,878 studies identified, removing the duplicates. After screening titles and abstracts, 109 articles remained for full-text assessment, of which 28 met the eligibility criteria for this systematic review[3,16-42]. Based on the study design, the papers were categorized as retrospective (n = 14), prospective (n = 4), and propensity score-matched (n = 10) studies. Figure 1 illustrates the PRISMA study selection flowchart.

Methodological quality

As shown in Table 1, most included studies were of moderate to high quality (NOS ≥ 6). Only four studies were designed as prospective analyses. Ten studies used propensity score-matched analysis to compare the surgical approaches. Half of the studies were conducted in the Western Countries. Laparoscopy was the

Table 1. Methodological quality of the manuscripts

Author	Study period	Country	Study design	*N* of patients		Details of MIS	Quality
				MILP	OLP		
Retrospective studies							
Anderson	2010-2012	USA	Retrospective	505	1,302	LLP (51)/RLP (454)	8
Chopra	2008-2019	USA	Retrospective	105	41	LLP (17)/RLP (88)	6
Hao	2013-2017	China	Retrospective	41	46	LLP	6
Huang	2014-2018	China	Retrospective	20	31	LLP	5
Hu	2007-2011	China	Retrospective	11	23	LLP	8
Hirashita	2007-2019	Japan	Retrospective	19	31	LLP	5
Kantor	2010-2013	USA	Retrospective	349	1,205	LLP	6
Kooby	2000-2008	USA	Retrospective	23	70	LLP	7
Magge	2002-2010	USA	Retrospective	28	34	LLP (20)/RLP (8)	8
Sharpe	2010-2011	USA	Retrospective	144	625	LLP	7
Sulpice	2007-2012	France	Retrospective	347	2,406	LLP	8
Zhang	2003-2013	China	Retrospective	17	34	LLP	7
Zhang	2012-2018	China	Retrospective	25	23	LLP	6
Zhang	2010-2014	China	Retrospective	22	76	LLP	6
Prospective studies							
Bauman	2005-2014	USA	Prospective	33	46	LLP (28)/RLP (5)	7
Plotkin	2011-2014	USA	Prospective	166	335	LLP (130)/RLP (36)	7
Shin	2006-2013	Korea	Prospective	70	80	LLP	8
Stauffer	1995-2014	USA	Prospective	44	28	LLP	7
Propensity score matching studies							
Balduzzi	2007-2015	Italy	Propensity score matching	44	44	LLP	8
Chen	2004-2020	China	Propensity score matching	86	86	LLP	6
Chen	2010-2019	China	Propensity score matching	66	66	LLP	7
Kwon	2010-2017	Korea	Propensity score matching	156	156	\	7
Lee	2007-2010	Korea	Propensity score matching	10	40	LLP (8)/RLP (4)	8
Lee	2009-2017	Korea	Propensity score matching	35	105	LLP	7
Raoof	2010-2013	USA	Propensity score matching	563	563	LLP	8
Van Hilst	2007-2015	Dutch	Propensity score matching	340	340	LLP (324)/RLP (16)	8
Watson	2010-2016	USA	Propensity score matching	805	805	\	8
Weng	2011-2019	China	Propensity score matching	170	166	RLP	8

MILP: Minimally invasive left pancreatectomy; OLP: open left pancreatectomy; MIS: minimally invasive surgery; LLP: laparoscopic left pancreatectomy; RLP: robotic left pancreatectomy.

most common minimally invasive approach used. Seven articles reported both, laparoscopic and robotic, surgical procedures, while only a recent Chinese paper compared robotic and OLPs.

Minimally invasive left pancreatectomy *vs.* open left pancreatectomy

A total of 28 studies on MILP *vs.* OLP were included in the systematic review. Overall, 4,254 and 8,807 patients were submitted to MILP and OLP, respectively. The growth of the minimally invasive approach is evidenced by the increased use of robotic platforms, with 660 robotic procedures reported in studies published after 2010, compared to 125 robotic distal pancreatectomies before 2010.

Few data were reported about the baseline and demographic characteristics of the patients [Supplementary Table 1]. Most studies reported no significant differences between the groups in terms of age, BMI, and ASA score. The open approach was preferred for surgical exploration post-chemotherapy, as reported in a

large series by Sharpe *et al.* and Plotkin *et al.* Conversion rate had a high variation across the studies ranging from 0% to 40%[25,31] [Supplementary Table 2]. Table 2 and Supplementary Table 2 summarize the intraoperative outcomes. Since the first study, the minimally invasive approach reported an improvement in the operating time and estimated blood loss. A recent propensity score-matching study from Weng *et al.* reported a significant reduction in the median operative time (120 *vs.* 180 min, $P < 0.001$) comparing the robotic approach to the OLP[43]. The better results were more evident in analyzing the estimated blood loss. Almost all the studies reported a decrease in blood loss during the MIDP across the study period. Indeed, considering two large propensity score-matching studies by Van Hilst *et al.* and Chen *et al.*, both reported significant improvements in the intraoperative bleeding control (200 *vs.* 300 mL, $P < 0.001$; 195 *vs.* 210 mL, $P < 0.01$, respectively)[35,40]. Major vessel resections were poorly described and, most of the time, involved venous resection and an open approach.

Regarding the postoperative outcomes, the use of the minimally invasive approach did not have any impact on the occurrence of major complications when compared to the OLP. Only large series, such as those by Sulpice *et al.* and Plotkin *et al.*, reported a favorable outcome in the minimally invasive group (6.6% *vs.* 10.4%, $P = 0.028$; 31.0% *vs.* 42.0%, $P = 0.024$, respectively)[26,31]. Pancreas-specific complications such as pancreatic fistula, post-pancreatectomy hemorrhage, and delayed gastric emptying were not affected by the surgical approach [Supplementary Table 3].

However, almost the entire cohorts reported in the literature recorded a lower hospital length of stay in the minimally invasive group across all the study designs and periods analyzed. Different minimally invasive approaches, whether laparoscopic or robotic, did not influence the reduction in hospitalization, as demonstrated by large series such as those by Kantor *et al.* (7.1 ± 6.0 *vs.* 8.7 ± 7.3 days, $P < 0.001$), and Weng *et al.* [14 (10-21) *vs.* 17 (12-24) days, $P = 0.001$][22,43].

Table 3 shows the oncological outcomes. The minimally invasive approach was not inferior when compared to OLP regarding the radical resection status. Furthermore, MILP appeared superior to OLP in achieving R0 status. Anderson *et al.* described a significant increase in the surgical margin disease-free of the minimally invasive resections compared to the open group (85.9% *vs.* 79.0%, $P < 0.001$)[16]. Overall, the harvested lymph node rate resulted appropriated, even higher in the minimally invasive group as described by Stauffer *et al.* (26 *vs.* 13, $P < 0.001$)[3]. Two studies by Van Hilst *et al.* and Weng *et al.* reported a significant decrease in the number of harvested lymph nodes during MILP (14 *vs.* 22, $P < 0.001$; 9 *vs.* 12, $P = 0.003$, respectively)[40,43].

The adjuvant treatment rate reported was surprisingly inferior to expectation. The different surgical approaches did not have any impact on this result, even if positive postoperative outcomes have been reported in the minimally invasive group. Comparable results were recorded for the overall postoperative survival. Overall, the surgical approach did not affect the patient's survival. However, a large series reported some long-term benefits of the MILP. Sulpice *et al.* analyzed 347 laparoscopic LP, describing a significant improvement in survival in the minimally invasive group (62.5 *vs.* 36.7 months, $P < 0.001$)[26]. These data were confirmed by two recent large series by Kwon *et al.* and Watson *et al.* that reported a higher overall survival rate of the MILP when compared to OLP (34.9 *vs.* 24.5 months, $P = 0.012$; 28.0 *vs.* 21.0 months, $P = 0.006$, respectively)[36,41].

DISCUSSION

Despite advances in surgical techniques and the widespread use of minimally invasive approaches for resecting benign and pre-malignant pancreatic tumors, pancreatic resection for adenocarcinoma remains a challenge, even in experienced hands[44].

Table 2. Intraoperative and postoperative outcomes

Author	Procedure	Operation time	*P* value	Blood loss	*P* value	CD > 2 complications	*P* value	Postoperative hospital stay	*P* value
Retrospective studies									
Anderson	MIS 505 Open 1,302	N.A.	\	N.A.	\	N.A.	\	6 (5-8) 7 (6-10)	**< 0.001**
Chopra	MIS 105 Open 41	280 (174-416) 248 (181-334)	**0.001**	181 (50-606) 200 (100-450)	0.119	23% 10%	0.414	6 (5-8) 7 (5.5-7)	0.695
Hao	LAP 41 Open 46	411.0 ± 106.2 355.8 ± 72.7	NS	294.4 ± 247.5 338.6 ± 230.0	0.410	3% 2%	0.500	7.9 ± 1.4 11.5 ± 2.7	**< 0.001**
Huang	LAP 20 Open 31	273.8 ± 90.3 264.3 ± 77.1	0.692	252.5 ± 198.3 472.6 ± 428.0	**0.037**	5% 3%	0.263	19.0 ± 9.9 19.6 ± 16.8	0.876
Hu	LAP 11 Open23	150.0 ± 54.0 160.0 ± 48.0	0.445	100 (50-400) 150 (50-350)	0.678	N.A.	\	5.2 ± 2.5 8.6 ± 3.9	**0.010**
Hirashita	LAP 19 Open 31	397.0 ± 78.0 319.0 ± 80.0	**0.001**	299.0 ± 237.0 576.0 ± 78.0	**0.034**	N.A.	\	21.5 ± 10.5 29.4 ± 23.3	0.171
Kantor	MIS 349 Open 1,205	N.A.	\	N.A.	\	N.A.	\	7.1 ± 6.0 8.7 ± 7.3	**< 0.001**
Kooby	LAP 23 Open 189	238.4 ± 68.1 230.4 ± 80.4	0.065	422.0 ± 473.0 790.0 ± 828.0	**0.040**	N.A.	\	7.4 ± 3.4 10.7 ± 6.3	**0.030**
Magge	MIS 28 Open 34	317.0 ± 23.0 294.0 ± 24.0	NS	290.0 ± 60.0 570.0 ± 80.0	**0.006**	0% 9%	0.730	6 (IQR: 3) 8 (IQR: 2.75)	**0.030**
Sharpe	LAP 144 Open 625	N.A.	\	N.A.	\	N.A.	\	6.8 ± 4.6 8.9 ± 7.5	**< 0.001**
Sulpice	LAP 347 Open 2,406	N.A.	\	N.A.	\	7% 10%	**0.028**	14.9 ± 8.9 19.6 ± 14.6	**< 0.001**
Zhang	LAP 25 Open 23	212.2 ± 66.3 203.1 ± 39.7	0.572	402.0 ± 258.8 506.5 ± 418.4	0.119	N.A.	\	11.7 ± 5.2 12.9 ± 5.0	0.425
Zhang	LAP 22 Open 76	188.0 ± 39.0 160.0 ± 35.0	0.060	210.0 ± 130.0 240.0 ± 120.0	0.240	N.A.	\	N.A.	\
Zhang	LAP 17 Open 34	190 (100-390) 245 (155-420)	0.064	50 (30-500) 400 (100-3,900)	**< 0.001**	0% 9%	0.754	13 (4-23) 15.5 (6-40)	**0.022**
Prospective studies									
Bauman	LAP 33 Open 46	234.0 ± 12.0 252.0 ± 12.0	0.360	310.0 ± 68.0 597.0 ± 95.0	**0.016**	15% 22%	0.100	7.6 ± 1.4 9.0 ± 0.7	0.440
Plotkin	MIS 166 Open 355	239.0 ± 9.0 250.0 ± 6.2	0.311	N.A.	\	10% 15%	**0.024**	5.0 ± 0.31 7.0 ± 0.51	**0.009**
Shin	LAP 70 Open 80	239 (125-397) 254 (115-573)	0.320	N.A.	\	20% 26%	0.310	9 (5-29) 12 (7-87)	**< 0.001**

Stauffer	LAP 44 Open 28	254 (99-521) 266 (131-543)	0.596	322 (10-2650) 874 (150-3,400)	**0.001**	14% 25%	0.346	5.1 (2-17) 9.4 (4-36)	**< 0.001**
Propensity score matching studies									
Balduzzi	LAP 44 Open 44	240 (195-322) 280 (222-379)	0.107	290 (70-650) 333 (130-700)	0.495	25% 34%	0.350	9 (6-13) 13 (8-23)	**0.005**
Chen	LAP 66 Open 66	193.6 ± 49.6 217.5 ± 61.0	**0.020**	195 (80-800) 210 (80-800)	**< 0.01**	6% 12%	0.500	12 (4-34) 15 (7-42)	**< 0.01**
Chen	LAP 86 Open 86	189.1 ± 45.2 213.3 ± 54.4	**< 0.01**	180 (80-600) 220 (120-800)	**< 0.01**	5% 11%	0.330	9 (4-34) 13 (7-42)	**< 0.01**
Kwon	MIS 156 Open 156	217 ± 56 222 ± 81	0.500	N.A.	\	6% 3%	0.190	10.0 ± 5.1 13.4 ± 7.9	**< 0.001**
Lee	MIS 10 Open 40	330.0 ± 168.2 253.3 ± 124.7	0.112	440.0 ± 328.0 625.0 ± 879.0	0.366	N.A.	\	12.7 ± 7.1 22.1 ± 27.1	**0.050**
Lee	LAP 35 Open 105	128.0 ± 40.0 170.0 ± 64.0	**0.001**	235.0 ± 240.0 252.0 ± 229.0	0.718	11% 15%	0.782	11.1 ± 6.7 14.4 ± 7.7	**0.026**
Raoof	LAP 563 Open 563	N.A.	\	N.A.	\	N.A.	\	6 (5-8) 7 (5-9)	**< 0.001**
Van Hilst	MIS 340 Open 340	240 (180-295) 230 (178-286)	0.626	200 (60-400) 300 (150-500)	**< 0.001**	18% 21%	0.431	8 (6-12) 9 (7-14)	**< 0.001**
Watson	MIS 805 Open 805	N.A.	\	N.A.	\	N.A.	\	6.8 ± 5.5 8.5 ± 7.3	**< 0.001**
Weng	Robotic 170 Open 166	120 (110-180) 180 (150-234)	**< 0.001**	100 (50-200) 200 (100-350)	**< 0.001**	N.A.	\	14 (10-21) 17 (12-24)	**0.001**

Bold values denote statistical significance at the $P < 0.05$ level. CD: Clavien-Dindo classification[12]; MIS: minimally invasive surgery; N.A.: not applicable; LAP: laparoscopic surgery; NS: not significant.

The results of this systematic review have revealed that MILP was safe and feasible even in the treatment of PDAC. The minimally invasive approach appears to be at least as effective as the open approach in terms of intra- and postoperative outcomes. Furthermore, the minimally invasive technique appeared to reduce both estimated blood loss and hospital length of stay. Regarding oncological outcomes, MILP again proved to be non-inferior when compared to OLP. Particularly, the MILP reached at least the same accuracy as the OLP in the lymphadenectomy and R0 resection.

Since the introduction of MIPS, there has been significant skepticism regarding its short- and long-term outcomes, especially compared to open surgery[45]. Nevertheless, this review clearly demonstrates a growing interest in MIPS over time. Increased use, standardization, and technological advancements have led to improved MIPS outcomes. Indeed, MILP, even when used in treating PDAC, showed advantages over open surgery, including reduced estimated blood loss (11/19 studies), shorter hospital stays (22/27 studies), comparable operative time (14/20 studies), and lower rates of major postoperative complications (15/18 studies).

Table 3. Oncological outcomes

Author	Procedure	R0 status	*P* value	Harvested LN	*P* value	Adjuvant chemotherapy	*P* value	Overall survival	*P* value
Retrospective studies									
Anderson	MIS 505 Open 1,302	85.9% 79.0%	**< 0.001**	12 (7-19) 12 (7-19)	0.350	57.8% 53.8%	0.110	3 years 55% 3 years 52%	0.420
Chopra	MIS 105 Open 41	69.5% 65.9%	0.538	24 (10-56) 20 (9-48)	0.077	77.0% 70.7%	0.628	33.5 months 28.4 months	0.914
Hao	LAP 41 Open 46	88.9% 81.8%	0.760	8.7 ± 6 8.4 ± 5.8	0.830	N.A.	\	24.0 months 21.0 months	0.090
Huang	LAP 20 Open 31	100.0% 97.0%	0.315	9.6 ± 6.4 12.8 ± 5.8	0.203	70.0% 80.6%	0.382	2 years 50.2% 2 years 38.3%	0.411
Hu	LAP 11 Open23	100.0% 100.0%	NS	14.8 ± 4.5 16.1 ± 5.7	0.875	N.A.	\	42.0 months 54.0 months	NS
Hirashita	LAP 19 Open 31	N.A.	\	14.0 ± 17.0 19.0 ± 18.0	0.845	68.0% 68.0%	NS	N.A.	0.084*
Kantor	MIS 349 Open 1,205	82.2% 75.1%	**< 0.001**	14.0 ± 11.7 14.8 ± 12.0	0.310	67.9% 61.8%	**0.050**	29.9 months 24.0 months	0.090
Kooby	LAP 23 Open 189	74.0% 73.0%	0.098	13.8 ± 8.4 12.5 ± 8.5	0.470	57.0% 70.0%	0.230	11.0 months 11.0 months	0.710
Magge	MIS 28 Open 34	86.0% 88.0%	NS	11 (8-20) 12 (6-19)	0.750	N.A.	\	N.A.	0.800*
Sharpe	LAP 144 Open 625	87.0% 78.0%	**0.042**	14.9 ± 10.0 13.3 ± 9.9	0.085	N.A.	\	N.A.	\
Sulpice	LAP 347 Open 2,406	N.A.	\	N.A.	\	N.A.	\	62.5 months 36.7 months	**< 0.001**
Zhang	LAP 25 Open 23	92.0% 95.6%	0.663	15.8 ± 6.7 18.2 ± 7.9	0.268	92.0% 82.6%	0.716	24.5 months 28.7 months	0.633
Zhang	LAP 22 Open 76	91.0% 87.0%	0.610	11.2 ± 4.6 14.4 ± 5.5	0.440	N.A.	\	29.6 months 27.6 months	0.340
Zhang	LAP 17 Open 34	94.1% 85.3%	0.650	9 (5-15) 8 (2-22)	0.534	76.5% 76.5%	NS	14.0 months 14.0 months	0.802
Prospective studies									
Bauman	LAP 33 Open 46	77.0% 87.0%	0.530	14.5 ± 1.1 17.5 ± 1.2	0.070	61.0% 63.0%	0.830	17.9 months 15.1 months	NS
Plotkin	MIS 166 Open 355	N.A.	\	N.A.	\	N.A.	\	N.A.	\
Shin	LAP 70 Open 80	75.7% 83.8%	0.220	12 (1-34) 10 (1-64)	0.130	78.6% 68.8%	0.180	33.4 months 29.1 months	0.250
Stauffer	LAP 44 Open 28	95.5% 82.1%	0.101	26 (5-48) 13 (1-45)	**< 0.001**	75.6% 75.0%	NS	26.6 months 26.4 months	0.851
Propensity score matching studies									
Balduzzi	LAP 44 Open 44	67.0% 48.0%	0.063	11 (6-22) 19 (11-30)	**0.023**	71.0% 79.0%	0.758	19 months 20 months	0.571
Chen	LAP 66 Open 66	97.0% 89.4%	**0.008**	13.4 ± 5.4 11.7 ± 5.1	0.006	71.2% 65.2%	0.460	19.0 months 17.0 months	0.330
Chen	LAP 86 Open 86	96.5% 90.7%	0.120	14.4 ± 5.2 12.7 ± 5.0	**0.030**	70.9% 66.3%	0.510	N.A.	0.500
Kwon	MIS 156 Open 156	76.3% 64.1%	**0.019**	14.1 ± 8.7 15.6 ± 9.7	0.150	66.7% 66.4%	NS	34.9 months 24.5 months	**0.012**
Lee	MIS 10 Open 40	100.0% 87.5%	0.426	11.7 ± 7.2 12.1 ± 8.1	0.887	70.0% 65.0%	0.765	N.A.	0.053*
Lee	LAP 35 Open 105	94.3% 90.5%	0.730	12.6 ± 8.1 14.3 ± 10.0	0.380	N.A.	\	N.A.	\
Raoof	LAP 563 Open 563	85.1% 81.5%	0.110	12 (7-18) 11 (6-18.5)	0.759	N.A.	\	3 years 41.6% 3 years 36.0%	0.457
Van Hilst	MIS 340 Open 340	67.0% 58.0%	**0.019**	14 (8-22) 22 (14-31)	**< 0.001**	76.0% 73.0%	0.561	28.0 months 31.0 months	0.774
Watson	MIS 805 Open 805	83.1% 80.0%	0.605	13.8 ± 10.3 14.2 ± 10.1	0.524	53.4% 51.6%	0.454	28.0 months 21.0 months	**0.006**

Weng	Robotic 170 Open 166	92.9% 89.2%	0.224	9 (4-14) 12 (7-17)	**0.003**	61.8% 67.5%	0.274	31.0 months 27.0 months	0.070

*Reported only the *P* value of the survival. Bold values denote statistical significance at the $P < 0.05$ level. LN: lymph node; MIS: minimally invasive surgery; LAP: laparoscopic surgery; N.A.: not applicable; NS: not significant.

For left-sided PDAC, the recommended oncological treatment includes resection of the spleen, Gerota's fascia, and appropriate lymphadenectomy (at least 11 lymph nodes with resection of stations 10, 11, and 18 for pancreatic tail tumors, also adding stations 8 and 9 in case of pancreatic body tumors)[46,47]. In a recent multicenter study involving 1,200 patients from 34 centers, resection of Gerota's fascia ($P = 0.019$), R0 resection ($P = 0.006$), and a decreased lymph node ratio ($P < 0.001$) were identified as positive prognostic factors for overall survival[46]. Furthermore, two systematic reviews involving PDAC patients who underwent MILP analyzed these oncological outcomes[48,49]. These studies were significantly small, including only 5 and 12 studies with a total of 261 and 1,506 patients, respectively. However, the surgical free resection margin rate and survival reported were similar between the two surgical approaches, though the evidence available was of low quality. In the present study, after reviewing 28 studies, both R0 resection and survival rates were comparable between MILP and OLP (no difference in 19/28 and 22/28 studies, respectively). Additionally, similar results were found when considering the lymph node harvest rate (no difference in 20/28 studies). These findings were supported by the results of the latest RCT on the oncological safety and feasibility of the MILP[50]. The DIPLOMA trial is an international multicenter study that provided the best evidence of the non-inferiority of MILP for radical resection margin rate compared to OLP[50]. Furthermore, the study assessed that the harvested lymph node rate was similar in both groups. MILP was correlated to longer operative times but provided better aesthetic results one year postoperatively. In line with the results of this review, the surgical approach did not affect other postoperative outcomes. However, the authors did not record any benefits for time to functional recovery, estimated blood loss, and length of hospital stay from MILP as has been described in previous RCT performed for all indications[51,52]. To date, three RCTs are ongoing to compare MILP *vs.* OLP in patients with PDAC: (1) the LAPAN study, promoted by the Japan Clinical Oncology Group study (jRCT 1031220705)[53]; (2) the NCT03792932 trial performed by the Fudan University in China; and (3) the NCT03957135 trial performed by the Seoul National University Hospital in Korea.

Oncological outcomes may be closely linked to surgical outcomes. Indeed, we can assume that a short length of stay and a short time to return to normal activity are associated with a higher adjuvant chemotherapy treatment rate. It is widely recognized that completing adjuvant chemotherapy after PDAC resection is associated with improved overall survival. Recently, a study on 2,440 patients treated with upfront surgery for PDAC, showed that at least 65% of patients did not receive chemotherapy after surgery. Only 7% of the patients completed the adjuvant chemotherapy, while 28% received incomplete treatment[54]. The results of this review underlined the shorter hospitalization of the patients submitted to MILP compared to OLP, recording the same major complication rate. However, no significant difference in adjuvant treatment was reported between the two approaches. This could be explained by the possibility that the MIPS series included smaller tumors in the minimally invasive arm, which may not require adjuvant treatment after neoadjuvant chemotherapy.

The present results should be read carefully due to several limitations and potential selection bias of the included studies. Indeed, the selection criteria for candidates undergoing MIDP varied across studies and are commonly linked to postoperative outcomes. Young patients, with low BMI, small lesions at the first stage, no vascular involvement, and without previous abdominal surgery are more often selected for MILP. The availability of robotic platforms may also contribute to selection bias. Third, the robotic procedures

could be performed only in high-volume centers by expert surgeons. Fourth, a clear definition of free surgical margin or R0 resection is unavailable. The heterogeneity of the definitions could affect the oncological data, especially the patient's survival, as previously reported[55]. Fifth, only one RCT was available. Despite efforts to report more comparable data, using a registry, prospective database, or propensity score matching studies, RCTs remain mandatory to assess the real benefit of MILP in patients affected by PDAC.

CONCLUSIONS

This literature review suggests that MILP is technically feasible and safe for treating pancreatic adenocarcinoma of the body and tail. MILP did not affect major complications but reduced hospitalization time. In terms of oncological outcomes, free surgical resection margin rate, lymph node harvested rate, use of adjuvant chemotherapy, and overall survival were not influenced by the surgical technique. Further prospective randomized trials are warranted to assess the oncological benefit of MILP in patients affected by PDAC.

DECLARATIONS

Authors' contributions

Conception and design: De Pastena M, Coppola A
Administrative support: De Pastena M, Coppola A
Provision of study materials or patients: De Pastena M, Coppola A
Collection and assembly of data: De Pastena M, Coppola A, Esposito A, Casciani F, Tufo A, Salvia R
Data analysis and interpretation: De Pastena M, Coppola A, Esposito A, Casciani F, Tufo A, Salvia R
Manuscript writing: De Pastena M, Coppola A, Esposito A, Casciani F, Tufo A, Salvia R
Final approval of manuscript: De Pastena M, Coppola A, Esposito A, Casciani F, Tufo A, Salvia R

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All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

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Consent for publication

Not applicable.

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