Surgery Today (2021) 51:194–203
https://doi.org/10.1007/s00595-020-02120-5

REVIEW ARTICLE

Minimally invasive surgery for pancreatic cancer

Yoshihiro Miyasaka[1,2] · Takao Ohtsuka[1,3] · Masafumi Nakamura[1]

Received: 22 June 2020 / Accepted: 29 June 2020 / Published online: 28 August 2020

Abstract
Pancreatic cancer is the most lethal malignancy of the digestive organs. Although pancreatic resection is essential to radically cure this refractory disease, the multi-organ resection involved, as well as sequelae such as glucose tolerance insufficiency and severe complications impose a heavy burden on these patients. Since the late twentieth century, minimally invasive surgery has become more popular for the surgical management of digestive disease and pancreatic cancer. Minimally invasive pancreatic resection (MIPR), including pancreaticoduodenectomy and distal pancreatectomy, is now a treatment option for pancreatic cancer. Some evidence suggests that MIPR for pancreatic cancer provides comparable oncological outcomes to open surgery, with some advantages in perioperative outcomes. However, as this evidence is retrospective, prospective investigations, including randomized controlled trials, are necessary. Because neoadjuvant therapy for resectable or borderline-resectable pancreatic cancer and conversion surgery for initially unresectable pancreatic cancer has become more common, the feasibility of MIPR after neoadjuvant therapy or as conversion surgery requires further assessment. It is expected that progress in surgical techniques and devices, as well as the standardization of surgical procedures and widespread educational programs will improve the outcomes of MIPR.

Keywords Pancreatic cancer · Pancreatic resection · Minimally invasive · Laparoscopic · Robotic

Introduction

Pancreatic cancer is associated with a dismal prognosis and a 5-year survival rate of only 9% [1]. At the rate its incidence is increasing, it is anticipated that by 2030, it will be the second leading cause of cancer-related death [2]. Despite advances in chemotherapy and chemoradiotherapy, pancreatic resection is essential to cure pancreatic cancer. However, the multi-organ resection that pancreatic resection requires, together with glucose tolerance insufficiency and severe complications such as postoperative pancreatic fistula, impose a heavy burden on patients. In the 1970s, the mortality rate after pancreaticoduodenectomy (PD) was approximately 20%, but progress in surgical procedures and devices, combined with better postoperative management, have decreased the rate to around 3% [3–5].

During the late twentieth century, minimally invasive surgery (MIS); namely, laparoscopic and robotic surgery, encompassed digestive surgery, with laparoscopic surgery in the 1980s and robotic surgery in the 1990s [6]. Although the initial indication for MIS was benign conditions such as appendicitis or cholelithiasis, it expanded gradually to include gastrointestinal cancers [7, 8]. The several advantages of MIS, such as reduced postoperative pain, fewer wound complications, and early postoperative recovery, made MIS an attractive treatment option for cancer. According to a recent national survey by the Japan Society for Endoscopic Surgery, more than 60% of colorectal cancers are now treated by MIS [9]. Even open pancreatic surgery is a challenging procedure for surgeons because of the retroperitoneal location, anatomical complexity, and proximity to major vessels, but now minimally invasive pancreatic resection (MIPR) is being performed in clinical practice. MIPR for benign or low-grade malignant tumors has several advantages over open pancreatic resection in perioperative

✉ Masafumi Nakamura
mnaka@surg1.med.kyushu-u.ac.jp

1 Department of Surgery and Oncology, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan

2 Department of Surgery, Fukuoka University Chikushi Hospital, Chikushino, Japan

3 Digestive Surgery, Breast and Thyroid Surgery, Graduate School of Medical Sciences, Kagoshima University, Kagoshima, Japan

outcomes [10]. According to a worldwide survey on MIPR, 90% of participating surgeons thought that MIPR had overall advantages for patients [11]. Thus, the application of MIPR to pancreatic cancer treatment may benefit patients with this refractory disease. To promote a better understanding of MIPR for pancreatic cancer, we review its history and current status, and discuss its future perspectives.

History of minimally invasive pancreatic resection for pancreatic cancer

Following the successful application of laparoscopy to several hepato-pancreato-biliary procedures such as cholecystectomy, choledochotomy, and liver resection, laparoscopic pancreatic resection was introduced [6]. In 1994, Gagner et al. reported their first laparoscopic PD (LPD) for chronic pancreatitis, performed in 1992 [12]. Then, in 1996, Cuschieri et al. described the first laparoscopic distal pancreatectomy (LDP), also performed for chronic pancreatitis [13]. The first description of MIPR for pancreatic cancer was in a case series of laparoscopic pancreatic resections (LPRs) reported by Gagner et al. in 1997 [14]. They reported 23 cases of LPR, four of which were LPD for pancreatic adenocarcinoma and one of which was LDP for pancreatic cystadenocarcinoma. The first description of robotic pancreatic resection for pancreatic cancer was in a case series reported by Giulianotti et al., who described three cases of robotic PD and three cases of robotic DP for pancreatic cancer [15]. The first case series of minimally invasive PD (MIPD) for pancreatic cancer, including oncological outcomes such as prognosis, was reported by Palanivelu et al. [16] in 2007, with 40 cases of LPD for periampullary malignancy, including nine for pancreatic adenocarcinoma and four for pancreatic cystadenocarcinoma. In the same year, Fernández-Cruz et al. [17] reported the first case series of minimally invasive DP (MIDP) for pancreatic cancer with oncological outcomes, including 13 cases of LDP performed for pancreatic cancer. They described the application of radical antegrade modular pancreatosplenectomy (RAMPS), which was proposed by Strasberg et al., to laparoscopic procedures for en bloc resection of left-sided pancreatic cancer in open surgery [18].

Current status of minimally invasive pancreatic resection for pancreatic cancer

The favorable perioperative outcomes of MIPR such as less blood loss and shorter hospital stay have resulted in MIPR becoming an accepted treatment option for pancreatic cancer in clinical practice. According to studies in the National Cancer Database (NCDB) of the United States, 27.9% (506/1807) of patients who underwent DP and 14.9% (1191/7967) of those who underwent PD for pancreatic cancer, were treated by minimally invasive approaches between 2010 and 2012 [19, 20]. In the National Comprehensive Cancer Network (NCCN) guidelines for pancreatic adenocarcinoma, MIS is described as equal to open surgery as a treatment option for resectable disease [21]. The Japanese Clinical Practice Guidelines for Pancreatic Cancer recommend LDP for pancreatic cancer except if there is multiple organ invasion or if combined vascular resection is required [22]. However, the Japanese guidelines state that LPD for pancreatic cancer is not recommended in clinical practice and should be performed in clinical studies. This is because LPD for cancer was not permitted by Japanese health insurance at the time of publication of the guidelines.

Several studies comparing MIPR and open pancreatic resection (OPR) for pancreatic cancer have been published. Tables 1, 2, 3 and 4 summarize these comparative studies between MIPR and OPR for pancreatic cancer (adenocarcinoma) [19, 20, 23–45]. All the studies were retrospective and ten of them collected data from nationwide databases including the NCDB [19, 20, 24, 28, 29, 34, 35, 37, 38, 42].

Table 1 compares the perioperative outcomes between MIDP and open distal pancreatectomy (ODP) [19, 23, 27, 28, 30, 32–36, 38–40, 42–44]. In most of these studies, operation time, postoperative complications, and mortality were comparable between MIDP and ODP, but MIDP was associated with less blood loss and a shorter hospital stay. Meta-analyses of comparative studies comparing MIDP and ODP for benign and malignant conditions also revealed less blood loss and a shorter hospital stay [10, 46, 47]. Although most studies showed comparable postoperative complication rates, two studies using nationwide databases revealed fewer postoperative complications after MIDP. Sulpice et al. [42] analyzed data from healthcare databases in France and found a significantly lower incidence of major abdominal complications after LDP. The study using data from the American College of Surgeons-National Surgical Quality Improvement Program identified a lower incidence of overall postoperative complications as well as pneumonia, surgical site infection, and sepsis [34]. The meta-analyses also showed reduced postoperative complications after MIDP [10, 46–48]. Thus, MIDP for pancreatic cancer may be associated with a lower incidence of postoperative complications. Table 2 compares the oncological outcomes of MIDP and ODP [19, 23, 27, 28, 30, 32, 33, 35, 36, 38–40, 42–44]. R0 resection rates, number of harvested lymph nodes, adjuvant chemotherapy, and overall survival were mostly comparable. Some large cohort studies revealed significantly higher R0 resection rates with MIDP [19, 28, 38, 43]. However, as bulky tumors or tumors close to major vessels tended to require open surgery rather than minimally invasive surgery in these studies, selection bias may have influenced the outcome. Meta-analyses of comparative studies between MIDP and ODP

Table 1 Perioperative outcomes of minimally invasive vs. open distal pancreatectomy for pancreatic cancer (adenocarcinoma)

Authors	Year	Procedure	Number of cases	Operation time (min)	*p* value	Blood loss (mL)	*p* value	Postoperative complication	*p* value	Mortality*	*p* value	Postoperative hospital stay	*p* value
Kooby et al. [30]	2010	Lap	23	238.4 ± 68.1	$p = 0.65$	422 ± 473	$p = 0.04$	NA	–	(30 d) 0%	NS	7.4 ± 3.4	$p = 0.03$
		Open	189	230.4 ± 80.4		790 ± 828		NA		(30 d) 1%		10.7 ± 6.3	
Magge et al. [33]	2013	MIS	28	317 ± 23	NS	290 ± 60	$p = 0.006$	39%	$p = 0.45$	0%	NS	6 (IQR: 3)	$p = 0.03$
		Open	34	294 ± 24		570 ± 80		50%		0%		8 (IQR: 2.75)	
Hu et al. [27]	2014	Lap	11	150.0 ± 54.0	$p = 0.445$	100 (50–400)	$p = 0.678$	NA	–	(30 d) 0%	NS	5.2 ± 2.5	$p = 0.010$
		Open	23	160 ± 48.0		150 (50–350)		NA		(30 d) 0%		8.6 ± 3.9	
Rehman et al. [36]	2014	Lap	8	376 (300–534)	$p = 0.009$	306 (250–535)	$p = 0.152$	37%	$p = 0.5$	(30 d) 12.5%	NS	8 (5–14)	$p = 0.05$
		Open	14	274 (180–420)		650 (145–1300)		42%		(30 d) 7.1%		12 (6–21)	
Lee et al. [32]	2014	MIS	10**	330 ± 168.2	$p = 0.112$	440 ± 382.1	$p = 0.366$	20%	$p = 0.441$	(30 d) 0%	$p = 0.448$	12.7 ± 7.1	$p = 0.05$
		Open	40**	253.3 ± 124.7		625.4 ± 878.8		32.5%		(30 d) 2.5%		22.1 ± 27.1	
Shin et al. [39]	2015	Lap	70	239 (125–397)	$p = 0.32$	NA	–	20%	$p = 0.31$	0%	NA	9 (5–29)	$p < 0.001$
		Open	80	254 (115–573)		NA		25.7%		1.2%		12 (7–87)	
Sulpice et al. [42]	2015	Lap	347	NA	–	NA	–	6.6%***	$p = 0.0284$	(90 d) 2.6%	$p = 0.0215$	14.9 ± 8.9	$p < 0.0001$
		Open	2406	NA		NA		10.4%***		(90 d) 5.6%		19.6 ± 14.6	
Sharpe et al. [38]	2015	Lap	144	NA	–	NA	–	NA	–	(30 d) 0%	$p = 0.222$	6.8 ± 4.6	$p < 0.001$
		Open	625	NA		NA		NA		(30 d) 2%		8.9 ± 7.5	
Zhang et al. [44]	2015	Lap	17	190 (100–390)	$p = 0.064$	50 (30–500)	$p = 0.000$	35.2%	$p = 0.754$	0%	NA	13 (4–23)	$p = 0.022$
		Open	34	245 (155–420)		400 (100–3900)		41.2%		2.9%		15.5 (6–40)	
Stauffer et al. [40]	2016	Lap	44	254 (99–521)	$p = 0.5961$	332 (10–2650)	$p = 0.0012$	13.6%****	$p = 0.3460$	(90 d) 2.3%	$p = 1.000$	5.1 (2–17)	$p = 0.0001$
		Open	28	266 (131–543)		874 (150–3400)		25%****		(90 d) 0%		9.4 (4–36)	
Anderson Jr et al. [19]	2017	MIS	505	NA	–	NA	–	NA	–	(90 d) 2.2%	$p = 0.43$	6 (5–8)	$p < 0.0001$
		Open	1302	NA		NA		NA		(90 d) 3.3%		7 (6–10)	
Plotkin et al. [34]	2017	MIS	166	239 ± 9.0	$p = 0.311$	NA	NA	31%	$p = 0.024$	(30 d) 0%	$p = 0.307$	5 ± 0.31	$p = 0.009$
		Open	335	250 ± 6.2		NA		42%		(30 d) 1%		7 ± 0.51	
Kantor et al. [28]	2017	Lap	349	NA	–	NA	–	NA	–	(90 d) 3.7%	$p = 0.26$	7.1 ± 6.0	$p < 0.01$
		Open	1205	NA		NA		NA		(90 d) 5.6%		8.7 ± 7.3	
Bauman et al. [23]	2018	Lap	33	3.9 ± 0.2 (h)	$p = 0.36$	310 ± 68	$p = 0.016$	52%	$p = 0.10$	(90 d) 3%	$p = 0.08$	7.6 ± 1.4	$p = 0.44$
		Open	46	4.2 ± 0.2 (h)		597 ± 95		70%		(90 d) 15%		9 ± 0.7	
Raoof et al. [35]	2018	Lap	563**	NA	–	NA	–	NA	–	(90 d) 2.8%	$p = 0.403$	6 (5–8)	$p < 0.001$
		Open	563**	NA		NA		NA		(90 d) 3.7%		7 (5–9)	
van Hilst et al. [43]	2019	MIS	340**	240 (180–295)	$p = 0.626$	200 (60–400)	$p < 0.001$	18%****	$p = 0.431$	(90 d) 2%	$p > 0.999$	8 (6–12)	$p < 0.001$
		Open	340**	230 (178–286)		300 (150–500)		21%****		(90 d) 3%		9 (7–14)	

Lap, laparoscopic only; MIS, laparoscopic and robotic

*(30 d): 30-day mortality rate, (90 d): 90-day mortality

**After propensity score matching

***Abdominal major complication

**** ≥ Clavien Dindo grade III

Table 2 Oncological outcomes of minimally invasive vs. open distal pancreatectomy for pancreatic cancer (adenocarcinoma)

Authors	Year	Procedure	Number of cases	R0 resection rate (%)	*p* value	Harvested LN	*p* value	Adjuvant chemotherapy(%)	*p* value	Overall survival	*p* value
Kooby et al. [30]	2010	Lap	23	74	$p=0.98$	13.8 ± 8.4	$p=0.47$	57	$p=0.23$	MST 11 months	$p=0.71$
		Open	189	73		12.5 ± 8.5		70		MST 11 months	
Magge et al. [33]	2013	MIS	28	86	$p>0.99$	11 (IQR: 8–20)	$p=0.75$	NA	–	NA	$p=0.80$*
		Open	34	88		12 (IQR: 6–19)		NA		NA	
Hu et al. [27]	2014	Lap	11	100	NS	14.8 ± 4.5	$p=0.875$	NA	–	42.0 ± 8.6 months	$p>0.05$
		Open	23	100		16.1 ± 5.7		NA		54.0 ± 5.8 months	
Rehman et al. [36]	2014	Lap	8	88	$p=0.794$	16 (1–27)	$p=0.53$	NA	–	MST 33 months	$p=0.91$
		Open	14	86		14 (0–26)		NA		MST 52 months	
Lee et al. [32]	2014	MIS	10**	100	$p=0.426$	11.7 ± 7.2	$p=0.887$	70	$p=0.765$	NA	$p=0.053$*
		Open	40**	87.5		12.1 ± 8.1		65		NA	
Shin et al. [39]	2015	Lap	70	75.7	$p=0.22$	12 (1–34)	$p=0.13$	78.6	$p=0.18$	MST 33.4 months	$p=0.25$
		Open	80	83.8		10 (1–64)		68.8		MST 29.1 months	
Sulpice et al. [42]	2015	Lap	347	NA	–	NA	–	NA	–	MST 62.5 months	$p<0.0001$
		Open	2406	NA		NA		NA		MST 36.7 months	
Sharpe et al. [38]	2015	Lap	144	87	$p=0.042$	14.9 ± 10.0	$p=0.085$	NA	–	NA	–
		Open	625	78		13.3 ± 9.9		NA		NA	
Zhang et al. [44]	2015	Lap	17	94.1	$p=0.650$	9 (5–15)	$p=0.534$	76.5	$p=1.000$	MST 14.0 months	$p=0.802$
		Open	34	85.3		8 (2–22)		76.5		MST 14.0 months	
Stauffer et al. [40]	2016	Lap	44	95.5	$p=0.1012$	25.9 (5–48)	$p=0.0001$	75.6	$p=1.000$	MST 26.6 months	$p=0.851$
		Open	28	82.1		12.7 (1–45)		75		MST 26.4 months	
Anderson Jr et al. [19]	2017	MIS	505	85.9	$p<0.001$	12 (7–19)	$p=0.35$	57.8	$p=0.11$	3 yr survival 55%	$p=0.42$
		Open	1302	79.0		12 (7–19)		53.8		3 yr survival 52%	
Kantor et al. [28]	2017	Lap	349	82.2	$p<0.001$	14.0 ± 11.7	$p=0.31$	67.9	$p=0.05$	MST 29.9 months	$p=0.09$
		Open	1205	75.1		14.8 ± 12.0		61.8		MST 24.0 months	
Bauman et al. [23]	2018	Lap	33	77	$p=0.53$	14.5 ± 1.1	$p=0.07$	61	$p=0.83$	MST 17.9 months	-
		Open	46	87		17.5 ± 1.2		63		MST 15.1 months	
Raoof et al. [35]	2018	Lap	563**	85.1	$p=0.110$	12 (7–18)	$p=0.759$	NA	–	3 yr OS 41.6%	$p=0.457$
		Open	563**	81.5		1 (6–18.5)		NA		3 yr OS 36.0%	
van Hilst et al. [43]	2019	MIS	340**	67	$p=0.019$	14 (8–22)	$p<0.001$	76%	$p=0.561$	MST 28 months	$p=0.774$
		Open	340**	58		22 (14–31)		73		MST 31 months	

Lap, laparoscopic only; MIS, laparoscopic and robotic

MST, median survival time; 3 yr OS, 3-year overall survival rate

*Although survival time was not provided, the results of comparative analysis of survival were shown

**After propensity score matching

Table 3 Perioperative outcomes of minimally invasive vs. open pancreaticoduodenectomy for pancreatic cancer (adenocarcinoma)

Authors	Year	Procedure	Number of cases	Operation time	*p* value	Blood loss	*p* value	Postoperative complication	*p* value	Mortality*	*p* value	Postoperative hospital stay	*p* value
Croome et al. [26]	2014	Lap	108	379.4 ± 93.5	$p = 0.45$	492.4 ± 519.3	$p < 0.001$	5.6%**	$p = 0.17$	(In Hp) 1%	$p = 0.50$	6 (4–118)	$p < 0.001$
		Open	214	387.6 ± 91.8		866.7 ± 733.7		13.6%**		(In Hp) 2%		9 (5–73)	
Sharpe et al. [37]	2015	Lap	384	NA	–	NA	–	NA	–	(30 d) 5.2%	$p = 0.163$	10 ± 8.0	$p < 0.0001$
		Open	4037	NA		NA		NA		(30 d) 3.7%		12 ± 9.7	
Nussbaum et al. [20]	2016	MIS	1191	NA	–	NA	–	NA	–	(90 d) 5.12%	$p = 0.22$	11.4 ± 10.3	$p < 0.01$
		Open	6776	NA		NA		NA		(90 d) 4.68%		12.3 ± 9.5	
Stauffer et al. [41]	2017	Lap	58	518 (313–761)	$p < 0.001$	250 (50–8500)	$p < 0.001$	53.4%	NS	(90 d) 5.2%	$p = 0.737$	6 (4–68)	$p < 0.001$
		Open	193	375 (159–681)		600 (50–7800)		66.8%		(90 d) 3.4%		9 (4–71)	
Kantor et al. [29]	2017	Lap	828	NA	–	NA	–	NA	–	(30 d) 4.1%	$p = 0.71$	10.2 ± 8.5	$p < 0.01$
		Open	7385	NA		NA		NA		(30 d) 3.8%		11.8 ± 9.3	
Chapman et al. [24]	2018	Lap	248	NA	–	NA	–	NA	–	(90 d) 7.2%	$p = 0.049$	10 (7–15)	$p = 0.06$
		Open	1520	NA		NA		NA		(90 d) 12.2%		10 (7–15.5)	
Kuesters et al. [31]	2018	Lap	62	477 (295–686)	$p < 0.001$	NA	–	53%	$p = 0.75$	(30 d) 4.8%	$p = 0.23$	14 (7–39)	$p = 0.03$
		Open	278	428 (245–714)		NA		55%		(30 d) 2.2%		16 (5–379)	
Zhou et al. [45]	2019	Lap	55***	330 (260–360)	$p < 0.001$	150 (100–200)	$p = 0.001$	49.1%	$p = 0.008$	(In Hp) 0%	$p = 0.530$	13 (11–20)	$p = 0.986$
		Open	93***	260 (207.5–325.5)		200 (150–350)		71.0%		(In Hp) 2.2%		14 (10–20)	
Choi et al. [25]	2020	Lap	27	477.7 ± 60.75	$p = 0.725$	232.59 ± 178.68	$p = 0.003$	NA	–	NA	–	21.19 ± 11.13	$p = 0.928$
		Open	34	471.21 ± 78.62		448.82 ± 343.83		NA		NA		19.94 ± 9.79	

Lap laparoscopic only; *MIS* laparoscopic and robotic

*(30 d): 30-day mortality rate, (90 d): 90-day mortality, (In Hp): in-hospital mortality

** ≥ Clavien Dindo grade IIIb

***After propensity score matching

Table 4 Oncological outcomes of minimally invasive vs. open pancreaticoduodenectomy for pancreatic cancer (adenocarcinoma)

Authors	Year	Procedure	Number of cases	R0 resection rate (%)	*p* value	Harvested LN	*p* value	Adjuvant chemotherapy (%)	*p* value	Overall survival	*p* value
Croome et al. [26]	2014	Lap	108	77.8	$p=0.81$	21.4 ± 8.1	$p=0.15$	76	$p=0.70$	MST 25.3 months	$p=0.12$
		Open	214	76.6		20.1 ± 7.5		76		MST 21.8 months	
Sharpe et al. [37]	2015	Lap	384	80	$p=0.026$	18 ± 9.7	$p=0.008$	NA	–	NA	–
		Open	4037	74		16 ± 9.6		NA		NA	
Nussbaum et al. [20]	2016	MIS	1191	79.8	$p=0.15$	17.4 ± 10.0	$p<0.01$	55.3	$p=0.08$	2 yr OS 43%	$p=0.36$
		Open	6776	77.9		16.5 ± 9.6		52.7		2 yr OS 47%	
Stauffer et al. [41]	2017	Lap	58	84.5	$p=0.426$	27 (9–70)	$p<0.001$	75.9	$p=0.858$	MST 18.5 months	$p=0.25$
		Open	193	79.8		17 (1–63)		73.5		MST 20.3 months	
Kantor et al. [29]	2017	Lap	828	79.1	$p=0.13$	18.1 ± 9.5	$p=0.01$	61.4	$p=0.87$	MST 20.7 months	$p=0.68$
		Open	7385	76.8		17.1 ± 9.6		60.4		MST 20.9 months	
Chapman et al. [24]	2018	Lap	248	77.4	$p=0.12$	NA	–	35.9	$p=0.98$	MST 19.8 months	$p=0.022$
		Open	1520	73.0		NA		36.0		MST 15.6 months	
Kuesters et al. [31]	2018	Lap	62	87	$p=0.01$	17 (7–28)	$p=0.69$	NA	–	5 yr OS 20%	$p=0.51$
		Open	278	71		16 (2–47)		NA		5 yr OS 14%	
Zhou et al. [45]	2019	Lap	55*	100	$p=0.201$	18 (13–25)	$p<0.001$	47.3	$p=0.701$	MST 20.0 months	$p=0.293$
		Open	93*	94.6		11 (7–14.5)		50.5		MST 18.7 months	
Choi et al. [25]	2020	Lap	27	92.59	$p=0.092$	13.33 ± 9.21	NS	77.78	$p=1.000$	MST 44.62 months	$p=0.223$
		Open	34	70.59		20.65 ± 9.47		79.41		MST 45.29 months	

Lap laparoscopic only; *MIS* laparoscopic and ro

MST, median survival time; *2 yr OS*, 2-year overall survival rate; *5 yr OS*, 5-year overall survival rate

*After propensity score matching

for pancreatic cancer also revealed comparable R0 resection rates, numbers of harvested lymph nodes, adjuvant chemotherapy, and overall survival except for one meta-analysis that showed a smaller number of harvested lymph nodes with MIDP [49–51].

Table 3 compares the perioperative outcomes of MIPD and open PD (OPD) [20, 24–26, 29, 31, 37, 41, 45]. Most studies showed similar postoperative complications and mortality after MIPD and OPD, but MIPD was associated with longer operation time, less blood loss, and a shorter hospital stay. MIPD was also associated with a longer operation time, less blood loss, and a shorter hospital stay in meta-analyses of studies comparing MIPD and OPD for benign and malignant periampullary disease [52, 53]. Although mortality was comparable for MIPD and OPD, a low hospital volume was associated with increased mortality in MIPD [37]. International Evidence-based Guidelines on MIPR recommend that MIPD should be performed at high-volume centers [54].

Table 4 compares the oncological outcomes of MIPD and OPD [20, 24–26, 29, 31, 37, 41, 45]. In most studies, MIPD and OPD showed comparable R0 resection rates, adjuvant chemotherapy, and overall survival, but MIPD achieved larger numbers of harvested lymph nodes. A meta-analysis of randomized controlled trials and high-quality nonrandomized studies comparing MIPD and OPD also showed a higher number of harvested lymph nodes in MIPD [53]. Magnified high-resolution images and meticulous manipulation of minimally invasive surgery may facilitate lymph node dissection.

RAMPS is often used in MIDP for pancreatic cancer [17, 32, 55, 56]. Medial-to-lateral dissection of the retroperitoneum in RAMPS may allow for a better laparoscopic view than the lateral-to-medial approach of conventional pancreatosplenectomy. Some surgeons use the ligament of Treitz approach to expose a dissection plane anterior to the left renal vein [57, 58]. Pancreatic cancer often requires combined vascular resection. Although some investigators have described MIPR with major vessel resection (portal vein resection or celiac axis resection) [59, 60], evidence of its safety and efficacy is limited. Therefore, it should be performed in high volume centers by experienced surgeons for the purpose of prospective investigations.

Future perspectives

Although MIPR for pancreatic cancer appears to be oncologically comparable to OPR and may have some better perioperative outcomes, the current evidence is based on retrospective studies. Further analyses according to prospective investigations including randomized controlled trials are necessary. Evidence of the usefulness of neoadjuvant therapy for resectable or borderline resectable pancreatic cancer is accumulating and the number of cases of conversion surgery for primary unresectable pancreatic cancer are increasing. However, the feasibility of MIPR after neoadjuvant therapy or as conversion surgery has not been established and requires further investigation.

MIPR for pancreatic cancer is still in development. Standardization of surgical procedures and widespread educational programs for MIPR may improve outcomes, as demonstrated by a nationwide training program in MIDP in the Netherlands, which reduced blood loss, conversion, margin-positive resection, and the length of hospital stay [61]. Further advances in imaging technology and surgical devices will also improve the precision of surgical procedures. For example, the application of augmented reality during MIPR may allow surgeons to locate tumors or vessels accurately despite the lack of tactile sensation [62]. Postoperative pancreatic fistula (POPF) is the most concerning complication of pancreatic surgery. A randomized controlled study suggested that stapler reinforcement may inhibit the development of POPF in distal pancreatectomy [63]. Thus, we await the development of methods or devices to overcome POPF.

The improvements in prognosis after pancreatic resection for pancreatic cancer resulting from better multidisciplinary treatments are unfortunately accompanied by an increasing number of cases of metachronous cancer in the remnant pancreas [64]. Several authors suggest that resection may improve the prognosis of patients with remnant pancreatic cancer [65–67]. If the initial pancreatic resection is performed by MIS, less adhesion is expected. One of the predictors of difficulty in laparoscopic repeat liver resection for recurrent hepatocellular carcinoma is the history of an open approach for the initial liver resection [68]. Hence, initial pancreatic resection according to MIS may facilitate secondary surgery for remnant pancreatic cancer.

Conclusion

MIPR for pancreatic cancer is being adopted in clinical practice more slowly than MIS for other abdominal malignancies. Current evidence suggests that it has some perioperative outcome advantages, with further advantages evolving through progress in techniques and devices. Whether MIPR benefits patient survival needs to be verified prospectively. Centralization, standardization, and education are future issues of MIPR for pancreatic cancer.

Compliance with ethical standards

Conflict of interest We have no conflict of interest to declare in association with this manuscript.

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