대학원 학위논문

A comparison of minimal invasive versus open pancreatectomy for pancreatic ductal adenocarcinoma in single institution

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의학과

권재우

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지도교수 : 김 송 철

이 논문을 석사 학위 논문으로 제출함

2018년 12월

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권재우의 석사학위 논문을 인준함.

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2018년 12월

목차

Introduction: Because of concerns about adequate oncological outcomes and perioperative complications, minimally invasive pancreatectomy (MIP) still has limitation of generalizability, and open pancreatectomy (OP) is preferred for pancreatic ductal adenocarcinoma (PDAC). Data is lacking, and differences in indication, perioperative outcomes, and oncologic outcomes between MIP and OP must be identified.

Methods: We retrospectively reviewed 1162 patients undergoing MIP and OP for PDAC from January 2011 to December 2017. We collected demographic, perioperative outcome, pathology, and overall and disease-free survival data and compared minimally invasive distal pancreatectomy (MIDP) and open distal pancreatectomy (ODP) as well as minimally invasive pancreaticoduodenectomy (MIPD) and open pancreaticoduodenectomy (OPD).

Result: We compared 184 MIDP patients with 179 ODP patients. MIDP and ODP patients differed for neoadjuvant chemotherapy (1.6% vs 14.0%, $p<0.001$) and concurrent vessel

resection (2.1% vs 18.4%, p<0.001). MIDP had shorter operation time (210 vs 236 min, p<0.001) and hospital stay (8 vs 11 days, p<0.001) than ODP. Other perioperative outcomes were the same. Pathologic outcome was not different between MIDP and ODP except lymphovasucular invasion (39.7% vs 53.6%, p=0.009) and harvested lymph node (14.0 vs 16.0, p=0.037). MIDP showed better survival than ODP in propensity-score matching (PSM) (HR=1.20, p=0.256) and inverse probability of treatment weight analysis (HR=1.43, p<0.001).

We also compared 76 MIPD patients with 723 OPD patients. MIPD and OPD patients differed for increased CA19-9 (50% vs 66.5%, p=0.013), proportion of mGPS (p=0.016), and vessel resection (15.8% vs 37.3%, p<0.001). MIPD had shorter hospital stay than OPD (10 vs 13 days, p<0.001). MIPD and OPD had different T stage, tumor size, and number of harvested and positive lymph nodes. After PSM, perioperative outcome and pathologic outcome were not different between MIPD and OPD. MIPD and OPD had the same overall survival after PSM.

Conclusion: A tendency to choose patients suitable for MIP remains; however, indications are increasing. MIDP had shorter operation time than ODP and MIP had shorter postoperative hospital stay than OP. MIDP and ODP had comparable pathologic outcomes and showed better survival for resectable PDAC. MIPD is feasible, can be performed safely and survival was also comparable to OPD in selected patients.

Table 1. Demographics of distal pancreatectomy

Variables		MIDP (n=184)	ODP (n=179)	P-value
Age, years	Mean	63.0	62.6	0.765
	Range	30.0–88.0	30.0–85.0	
Sex, n (%)	Female	80 (43.5)	80 (44.7)	0.833
	Male	104 (56.5)	99 (55.3)	
BMI, kg/m^2	Mean	23.5	23.2	0.369
	Range	16.5–31.7	15.7–31.7	
ASA score, n (%)	I	21 (11.4)	16 (8.9)	0.758
	II	153 (83.2)	153 (85.5)	
	III	10 (5.4)	10 (5.6)	
CA 19-9, n (%)	Normal	71 (38.6)	70(39.1)	0.828
	Increased	112 (60.9)	103 (57.5)	
	NA	1 (0.5)	6 (3.4)	
CEA, n (%)	Normal	157 (85.3)	146 (81.6)	0.755
	Increased	23 (12.5)	24 (13.4)	
	NA	4 (2.2)	9 (5.0)	
mGPS, n (%)	0	127 (69.0)	119 (66.5)	0.902
	1	9 (4.9)	8 (4.5)	
	2	2 (1.1)	14 (7.8)	
	NA	46(25)	38 (21.2)	
Neoadjuvant, n (%)	No	181 (98.4)	154 (86.0)	<0.001
	Yes	3 (1.6)	25 (14.0)	
Concurrent vessel resection, n (%)	Vein	3 (1.6)	15 (8.4)	<0.001
	Artery	1 (0.5)	10 (5.6)	

	Artery and Vein	0 (0.0)	8 (4.5)	
	No	180 (97.8)	146 (81.6)	
Concurrent resection	Yes	31 (16.8)	43 (24.0)	0.092
of other organ, n (%)	No	153 (83.2)	136 (76.0)	

BMI, body mass index; NA, not available; mGPS, modified Glasgow prognostic score

Table 2. Perioperative and pathologic outcome according to operation method of distal pancreatectomy

Variables		MIDP (n=184)	ODP (n=179)	P-value
Operation time, minutes	Mean	210	236	<0.001
	Range	83–444	25–585	
Hospital stay after operation, days	Median	8	11	<0.001
	IQR	5–40	6–80	
POPF[+], n, (%)[+]	No	135 (73.4)	131 (73.2)	0.629
	Biochemical leakage	26 (14.1)	23 (12.8)	
	Grade B	22 (12.0)	20 (11.2)	
	Grade C	1 (0.5)	5 (2.8)	
Complications grade[++], n (%)	No	115 (62.5)	114 (63.7)	0.410
	Grade I	34 (18.5)	18 (10.1)	
	Grade II	22 (12.0)	32 (17.9)	
	Grade III	13 (7.1)	13 (7.3)	
	Grade IV	0 (0)	1 (0.6)	
	Grade V	0 (0)	1 (0.6)	
Mortality (90 day in hospital), n (%)	No	183 (99.5)	176 (98.3)	0.366
	Yes	1 (0.5)	3 (1.7)	
Adjuvant	No	62 (33.7)	64 (35.8)	0.727
	CTx	95 (51.6)	85 (47.5)	
	CCRTx	27 (14.7)	30 (16.8)	
Pathologic tumor size, (cm)	Mean	3.3	3.5	0.213
	Range	0.4–8.5	0.1–11.0	

Staging (AJCC 8th)*, n (%)	IA	23 (12.5)	18 (10.1)	0.141
	IB	42 (22.8)	33 (18.4)	
	IIA	17 (9.2)	11 (6.1)	
	IIB	63 (34.2)	76 (42.5)	
	III	29 (15.8)	29 (16.2)	
	IV	10 (5.4)	12 (6.7)	
Differentiation	WD	22 (12.0)	17 (9.8)	0.713
	MD	131 (71.2)	135 (75.4)	
	PD	24 (13.0)	23 (12.8)	
	NA	7 (3.8)	4 (2.2)	
Lymphovascular invasion, n (%)	Yes	73 (39.7)	96 (53.6)	0.009
	No	111 (60.3)	83 (46.4)	
Perineural invasion, n (%)	Yes	147 (79.9)	141 (78.8)	0.797
	No	37 (20.1)	38 (21.2)	
Number of harvested lymph nodes, n	Mean	14.0	16.0	0.037
	Range	1–46	0–54	
Number of positive lymph nodes, n	Mean	1.7	1.6	0.507
	Range	0–14	0–9	
Lymph node ratio, %	Mean	12.0	11.3	0.637
	Range	0–75	0–57	
Resection margin**, n (%)	R0	134 (72.8)	115 (64.2)	0.090
	R1	50 (27.2)	64 (35.8)	

+ POPF was graded according to the definition updated in 2016 by International Study Group Pancreatic Fistula[19]

++ Complication grade was classified according to the Clavien-Dindo classification[20]

* TNM stage was graded according to American Joint Committee on Cancer stage 8th edition

** If closest safe resection margin was less than 1 mm, it was categorized as R1

POPF, postoperative pancreatic fistula; CTx, chemotherapy; CCRTx, concurrent chemoradiation therapy; WD, well differentiated; MD, moderately differentiated; PD, poorly differentiated; NA, not available

Table 3. Demographics of MIDP (n=118) and ODP (n=118) after propensity score matching

Variables		MIDP (n=118)	ODP (n=118)	SMD
Age, years	Mean	64.3	63.9	-0.035
Sex, n (%)	Female	54 (45.8)	50 (42.4)	0.068
	Male	64 (54.2)	68 (57.6)	
BMI, kg/m^2	Mean	23.45	23.40	-0.015
ASA score, n (%)	I	16 (13.6)	11 (9.3)	0.102
	II	95 (80.5)	100 (84.7)	
	III	7 (5.9)	7 (5.9)	
CA 19-9, n (%)	Normal	44 (37.3)	47 (39.8)	-0.087
	Increased	74 (62.7)	66 (55.9)	
	NA	0 (0)	5 (4.2)	
mGPS, n (%)	0	80 (67.8)	81 (68.6)	0.029
	1	10 (8.5)	4 (3.4)	
	2	2 (1.7)	7 (5.9)	
	NA	26 (22.0)	26 (22.0)	
Concurrent resection of other organ, n (%)	Yes	29 (24.6)	31 (26.3)	0.039
	No	89 (75.4)	87 (73.7)	

BMI, body mass index; NA, not available; mGPS, modified Glasgow prognostic score

Table 4. Perioperative and pathologic outcome of MIDP (n=118) and ODP (n=118) after propensity score matching

Variables		MIDP (n=118)	ODP (n=118)	P-value
Operation time, minutes	Mean	204	224	0.029
Hospital stay after operation, days	Mean	8.5	10.5	<0.001
Adjuvant	No	45 (38.1)	43 (36.4)	0.580
	CTx	56 (47.5)	53 (44.9)	
	CCRTx	17 (14.4)	22 (18.6)	
Staging (AJCC 8th)*, n (%)	IA	17 (14.4)	10 (8.5)	0.060
	IB	26 (22.0)	25 (21.2)	
	IIA	13 (11.0)	8 (6.8)	
	IIB	43 (36.4)	46 (39.0)	
	III	14 (11.9)	20 (16.9)	
	IV	5 (4.2)	9 (7.6)	
Lymphovascular invasion, n (%)	Yes	45 (38.1)	66 (55.9)	0.009
	No	73 (61.9)	52 (44.1)	
Perineural invasion, n (%)	Yes	94 (79.7)	91 (77.1)	0.752
	No	24 (20.3)	27 (22.9)	
Number of harvested lymph nodes, n	Mean	14.3	15.2	0.476
Lymph node ratio, %	Mean	10.69	12.37	0.390
Resection margin^{+}, n (%)	R0	87 (73.7)	75 (63.6)	0.122
	R1	31 (26.3)	43 (36.4)	

* TNM stage was graded according to American Joint Committee on Cancer stage 8th edition

+ If closest safe resection margin was less than 1 mm, it was categorized as R1

Table 5. Hazard ratio for overall survival and disease-free survival after propensity-score matching of distal pancreatectomy.

Propensity score match				Propensity score IPTW			
	95% CI				95% CI		
HR	Lower	Upper	p-value	HR	Lower	Upper	p-value
1.203	0.875	1.653	0.256	1.425	1.176	1.7	0.0003
1.265	0.936	1.709	0.126	1.439	1.2	1.724	<0.001

IPTW, inverse probability of treatment weight; CI, confidence interval; HR, hazard ratio

Table 6. Demographics of pancreaticoduodenectomy

Variables		MIPD (n=76)	OPD (n=723)	P-value
Age, years	Mean	62.2	61.6	0.646
	Range	35.0–80.0	32.0–85.0	
Sex, n (%)	Female	34 (44.7)	278 (38.5)	0.285
	Male	42 (55.3)	445 (61.5)	
BMI, kg/m^2	Mean	22.7	22.7	0.858
	Range	17.5–28.7	14.7–33.1	
ASA score, n (%)	I	8 (10.5)	46 (6.4)	0.119
	II	60 (78.9)	632 (87.4)	
	III	8 (10.5)	45 (6.2)	
CA 19-9, n (%)	Normal	34 (44.7)	229 (31.7)	0.013
	Increased	38 (50.0)	481 (66.5)	
	NA	4 (5.3)	13 (1.8)	
CEA, n (%)	Normal	53 (69.7)	573 (79.3)	0.869
	Increased	13 (17.1)	132 (18.3)	
	NA	10 (13.2)	18 (2.5)	
Preoperative biliary drainage, n (%)	NO	40 (52.6)	276 (38.2)	0.087
	PTBD	5 (6.6)	63 (8.7)	
	ERBD	27 (35.5)	313 (43.3)	
	ENBD	4 (5.3)	71 (9.8)	

mGPS, n (%)	0	56 (73.7)	475(65.7)	0.016
	1	9 (11.8)	42 (5.8)	
	2	8 (10.5)	98 (13.6)	
	NA	3 (3.9)	108 (14.9)	
Neoadjuvant, n (%)	No	70 (92.1)	670 (92.7)	1.000
	Yes	6 (7.9)	53 (7.3)	
Concurrent vessel resection, n (%)	Vein	11 (14.5)	224 (31.0)	<0.001
	Artery	1 (1.3)	32 (4.4)	
	Artery and Vein	0 (0)	14 (1.9)	
	No	64 (84.2)	453 (62.7)	
Concurrent resection of other organ, n (%)	Yes	0 (0)	22 (3.0)	0.256
	No	76 (100)	701 (97.0)	

BMI, body mass index; NA, not available; PTBD, percutaneous transhepatic biliary drainage; ENBD, endoscopic nasobiliary drainage; ERBD, endoscopic retrograde biliary drainage; mGPS, modified Glasgow prognostic score

Table 7. Perioperative and pathologic outcome according to operation method of pancreaticoduodenectomy

Variables		MIPD (n=76)	OPD (n=723)	P-value
Operation time, minutes	Mean	392	385	0.578
	Range	168–643	157–858	
Hospital stay after operation, days	Median	10	13	<0.001
	IQR	7–37	6–94	
POPF[+], n, (%)[+]	No	62 (81.6)	639 (88.4)	0.623
	Biochemical leakage	13 (17.1)	51 (7.1)	
	Grade B	1 (1.3)	30 (4.1)	
	Grade C	0 (0)	3 (0.4)	
Complications grade[++], n (%)	No	47 (61.8)	476 (65.8)	0.185
	Grade I	13 (17.1)	104 (14.4)	
	Grade II	5 (6.6)	111 (15.4)	
	Grade III	10 (13.2)	25 (3.5)	
	Grade IV	1 (1.3)	7 (1.0)	
	Grade V	0 (0)	0 (0)	
Mortality (90 day in hospital), n (%)	No	76 (100)	718 (99.3)	1.000
	Yes	0 (0)	5 (0.7)	
Adjuvant	No	15 (19.7)	238 (32.9)	0.047
	CTx	44 (57.9)	351 (48.5)	
	CCRTx	17 (22.4)	134 (18.5)	
Pathologic tumor size, (cm)	Mean	2.7	3.1	0.008
	Range	0.7–4.5	0–8.3	

T stage (AJCC 8th)*, n(%)	T1	17 (22.4)	95 (13.1)	0.004
	T2	55 (72.4)	526 (72.8)	
	T3	4 (5.3)	95 (13.1)	
	T4	0 (0)	7 (1.0)	
Staging (AJCC 8th)*, n (%)	IA	11 (14.5)	52 (7.2)	0.113
	IB	16 (21.1)	181 (25.0)	
	IIA	3 (3.9)	26 (3.6)	
	IIB	36 (47.4)	299 (41.4)	
	III	9 (11.8)	144 (19.9)	
	IV	1 (1.3)	21 (2.9)	
Lymphovascular invasion, n (%)	Yes	50 (65.8)	455 (62.9)	0.708
	No	26 (34.2)	268 (37.1)	
Perineural invasion, n (%)	Yes	53 (69.7)	651 (90.0)	<0.001
	No	23 (30.3)	72 (10.0)	
Number of harvested lymph nodes, n	Mean	18.6	22.2	0.007
	Range	2–53	1–68	
Number of positive lymph nodes, n	Mean	1.5	2.1	0.018
	Range	0–11	0–24	
Lymph node ratio, %	Mean	9.9	10.3	0.801
	Range	0–100	0–100	
Resection margin**, n (%)	R0	57 (75.0)	522 (72.2)	0.686
	R1	19 (25.0)	201 (27.8)	

+ POPF was graded according to the definition updated in 2016 by International Study Group Pancreatic Fistula[19]

++ Complication grade was classified according to the Clavien-Dindo classification[20]

POPF, postoperative pancreatic fistula; CTx, chemotherapy; CCRTx, concurrent chemoradiation therapy

* TNM stage was graded according to American Joint Committee on Cancer stage 8th edition

** If closest safe resection margin was less than 1 mm, it was categorized as R1

WD, well differentiated; MD, moderately differentiated; PD, poorly differentiated; NA, not available

Table 8. Demographics of MIPD (n=76) and OPD (n=76) after propensity score matching

Variables		MIPD (n=76)	OPD (n=76)	SMD
Age, years	Mean	62.2	62.2	0.054
Sex, n (%)	Female	34 (44.7)	35 (46.0)	0.026
	Male	42 (55.3)	41 (54.0)	
BMI, kg/m^2	Mean	22.7	22.7	-0.002
ASA score, n (%)	I	8 (10.5)	6 (7.9)	-0.059
	II	60 (78.9)	62 (81.6)	
	III	8 (10.5)	8 (10.5)	
CA 19-9, n (%)	Normal	34 (44.7)	37 (48.7)	0.146
	Increased	38 (50.0)	37 (48.7)	
	NA	4 (5.3)	2 (2.6)	
mGPS, n (%)	0	56 (73.7)	57 (75.0)	0.074
	1	9 (11.8)	9 (11.8)	
	2	8 (10.5)	8 (10.5)	
	NA	3 (3.9)	2 (2.6)	
Neoadjuvant, n (%)	No	70 (92.1)	66 (86.8)	-0.172
	Yes	6 (7.9)	10 (13.2)	

BMI, body mass index; NA, not available; mGPS, modified Glasgow prognostic score

Table 9. Perioperative and pathologic outcome of MIPD (n=76) and OPD (n=76) after propensity score matching

Variables		MIDP (n=76)	ODP (n=76)	P-value
Operation time, minutes	Mean	392	381	0.507
Hospital stay after operation, days	Mean	12.3	14.0	0.063
Adjuvant	No	15 (19.7)	43 (28.9)	0.226
	CTx	44 (57.9)	53 (52.6)	
	CCRTx	17 (22.4)	22 (18.4)	
Pathologic tumor size, (cm)	Mean	2.7	2.8	0.809
T stage (AJCC 8th)*, n(%)	T1	17 (22.4)	13 (17.1)	0.725
	T2	55 (72.4)	61 (80.3)	
	T3	4 (5.3)	2 (2.6)	
	T4	0 (0)	0 (0.0)	
Staging (AJCC 8th)*, n (%)	IA	11 (17.5)	7 (9.2)	0.259
	IB	16 (21.1)	18 (23.7)	
	IIA	3 (3.9)	0 (0.0)	
	IIB	36 (47.4)	36 (47.4)	
	III	9 (11.8)	11 (14.5)	
	IV	1 (1.3)	4 (5.3)	
Lymphovascular invasion, n (%)	Yes	50 (65.8)	46 (60.5)	0.503
	No	26 (34.2)	30 (39.5)	
Perineural invasion, n (%)	Yes	53 (69.7)	63 (82.9)	0.057
	No	23 (30.3)	13 (17.1)	

Number of harvested lymph nodes, n	Mean	18.6	20.0	0.412
Number of positive lymph nodes, n	Mean	1.5	1.8	0.350
Lymph node ratio, %	Mean	9.28	10.76	0.538
Resection margin[+], n (%)	R0	57 (75.0)	53 (69.7)	0.470
	R1	19 (25.0)	23 (30.3)	

[*] TNM stage was graded according to American Joint Committee on Cancer stage 8th edition

[+] If closest safe resection margin was less than 1 mm, it was categorized as R1

Table 10. Hazard ratio for overall survival and disease-free survival after propensity-score matching of pancreaticoduodenectomy

Propensity score match				Propensity score IPTW			
	95% CI				95% CI		
HR	Lower	Upper	p-value	HR	Lower	Upper	p-value
1.300	0.726	2.329	0.257	1.354	0.948	1.933	0.095
1.357	0.833	2.211	0.405	1.350	1.019	1.789	0.037

IPTW, inverse probability of treatment weight; CI, confidence interval; HR, hazard ratio

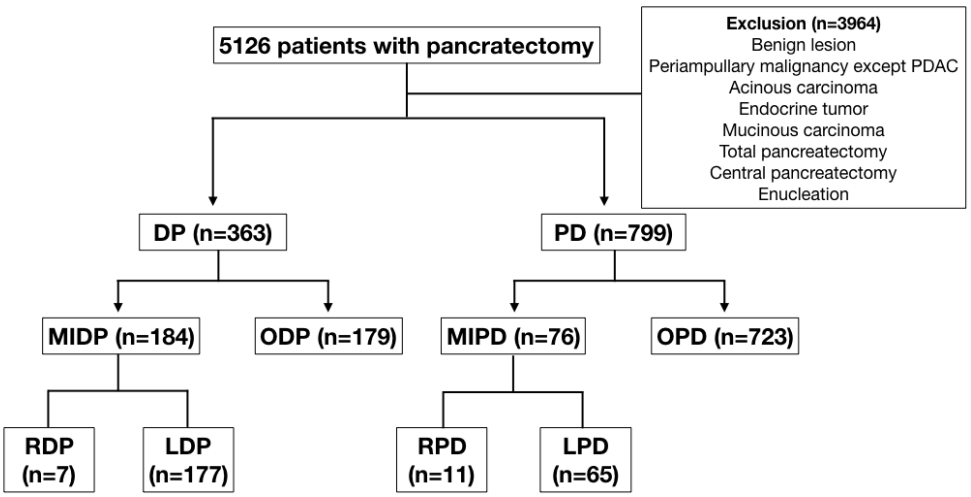

Figure 1. Patient flow diagram. We conducted a retrospective review of 1162 patients who underwent pancreatectomy after excluding 3964 patients based on exclusion criteria. Of these, 363 patients underwent DP and 799 patients, PD. The patients were categorized according to minimally invasive surgery and open surgery. Subgroup analysis was also performed.

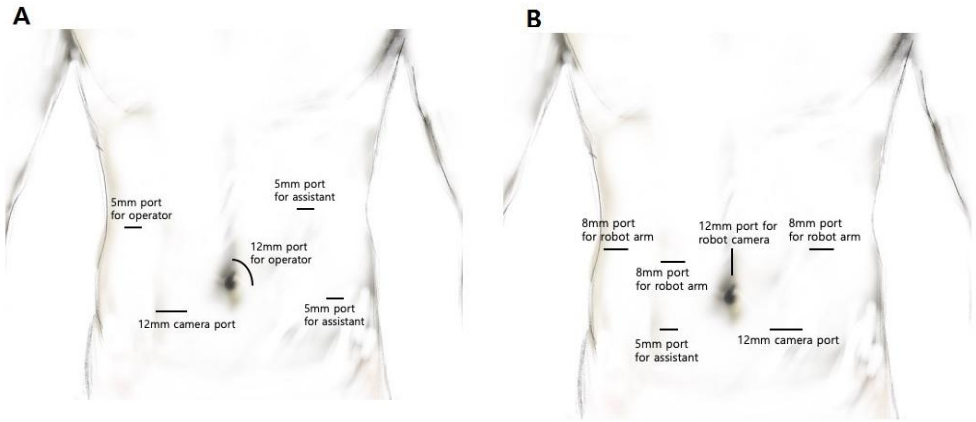

Figure 2. Trocar location of MIPD. (A) Port locations for LPD and RPD performed by laparoscopic resection and anastomosis by robot instrument. (B) Port locations for RPD performed by robotic resection and anastomosis.

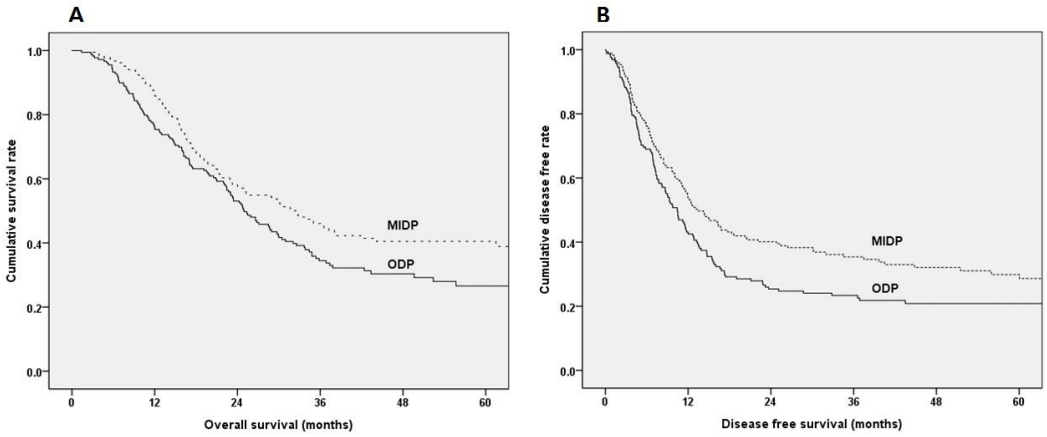

Figure 3. Kaplan-Meier survival curves of MIDP group (n=184) and ODP group (n=179). (A) The median OS and estimated 1-, 2-, and 5-year OS were respectively 32.6 months, 85.9%, 58.2%, and 40.5% in MIDP group and 25.0 months, 76.0%, 53.1%, and 26.6% in ODP group ($p = 0.023$). (B) The median DFS and estimated 1-, 2-, and 5-year DFS were respectively 13.3 months, 53.2%, 39.5%, and 28.6% in MIDP group and 10.4 months, 42.5%, 24.7%, and 20.8% in ODP group ($p = 0.020$).

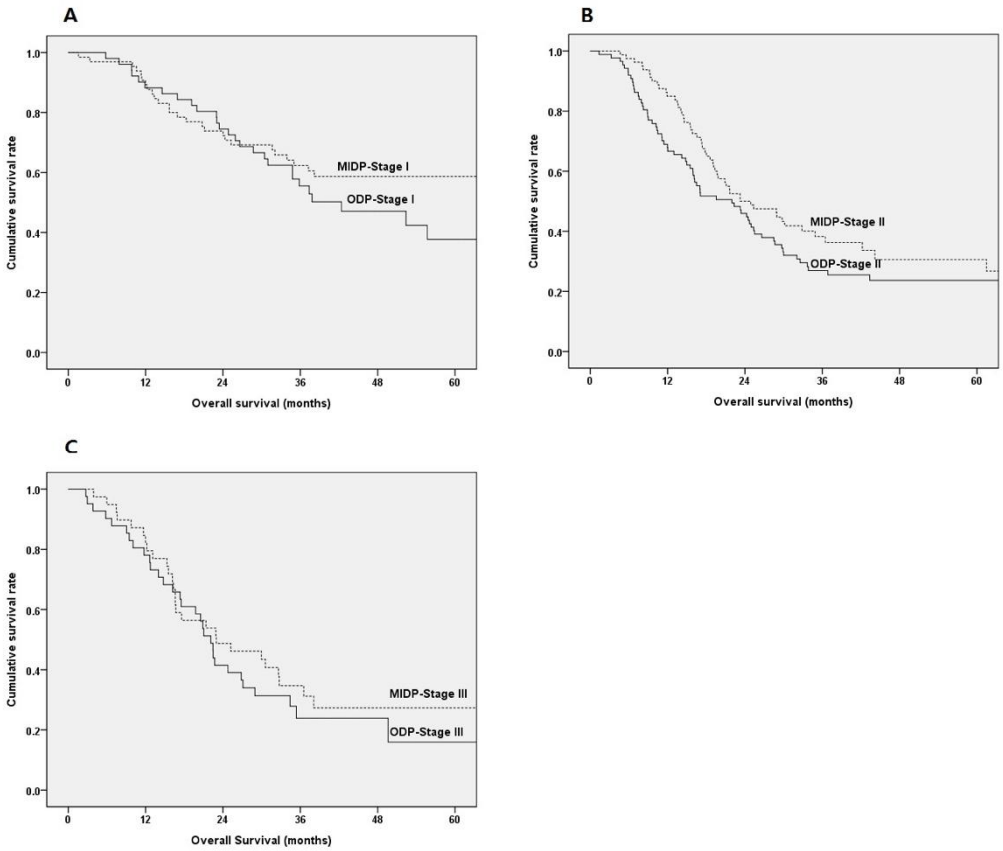

Figure 4. Kaplan-Meier survival curves of MIDP and ODP group according to AJCC 8th stage. (A) The median OS and estimated 1-, 2-, and 5-year OS were respectively 84.0 months, 89.2%, 73.8%, and 58.7% in stage I MIDP group (n=65) and 42.4 months, 88.2%, 74.5%, and 37.7% in stage I ODP group (n=51) (p = 0.283). (B) The median OS and estimated 1-, 2-, and 5-year OS were respectively 23.3 months, 85.0%, 50.0%, and 30.6% in stage II MIDP group (n=80) and 22.0 months, 67.8%, 46.0%, and 23.7% in stage II ODP group (n=87) (p = 0.101). (C) The median OS and estimated 1-, 2-, and 5-year OS were

respectively 23.0 months, 82.1%, 48.7%, and 27.3% in stage III MIDP group (n=39) and 22.1 months, 78.0%, 41.5%, and 15.9% in stage III ODP group (n=41) (p = 0.394).

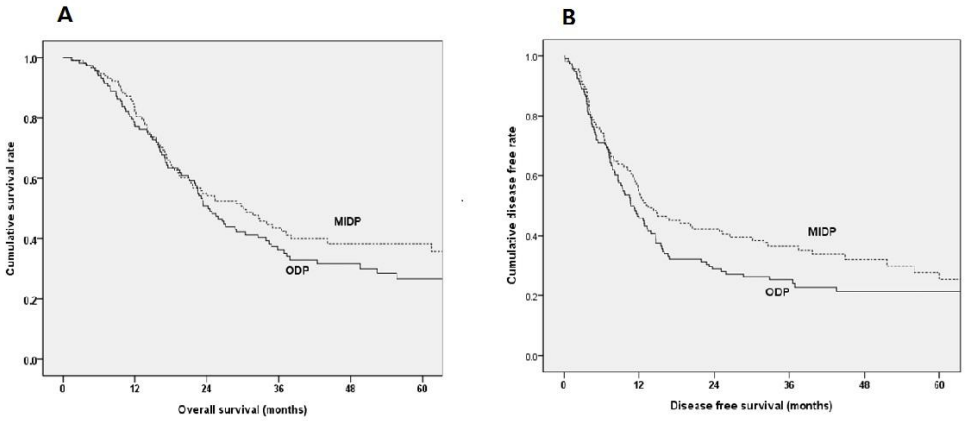

Figure 5. Kaplan-Meier survival curves of MIDP group (n=118) and ODP group (n=118) after propensity score matching. (A) The median OS and estimated 1-, 2-, and 5-year OS were respectively 30.2 months, 82.2%, 55.1%, and 38.4% in MIDP group and 24.2 months, 78.0%, 51.7%, and 26.8% in ODP group (p = 0.254). (B) The median DFS and estimated 1-, 2-, and 5-year DFS were respectively 13.5 months, 54.5%, 42.3%, and 27.6% in MIDP group and 10.6 months, 46.6%, 28.8%, and 21.3% in ODP group (p = 0.125).

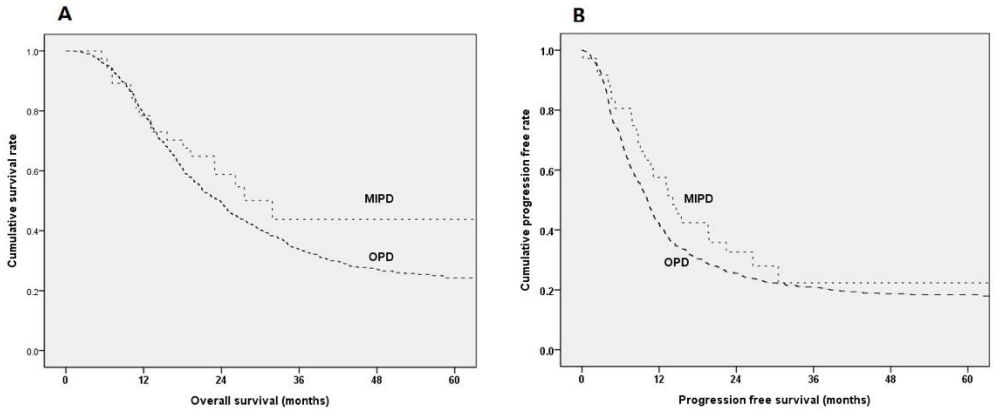

Figure 6. Kaplan-Meier survival curves of MIPD group (n=76) and OPD group (n=723). (A) The median OS was 31.87 months, and estimated 1-, 2-, 5- year OS were 75.7%, 54.6%, 43.8 % respectively, in MIPD group and 23.8 months and 79.1%, 49.4%, 23.7 % respectively, in OPD group. Log rank p-value was 0.182. (B) The median PFS was 14.1 months, and estimated 1-, 2-,5- year PFS were 55.8%, 30.3%, 25.2% respectively, in MIPD group, and 9.3 months and 41.8%, 25.4% , 17.9 % respectively, in OPD group. Log rank p-value was 0.119.

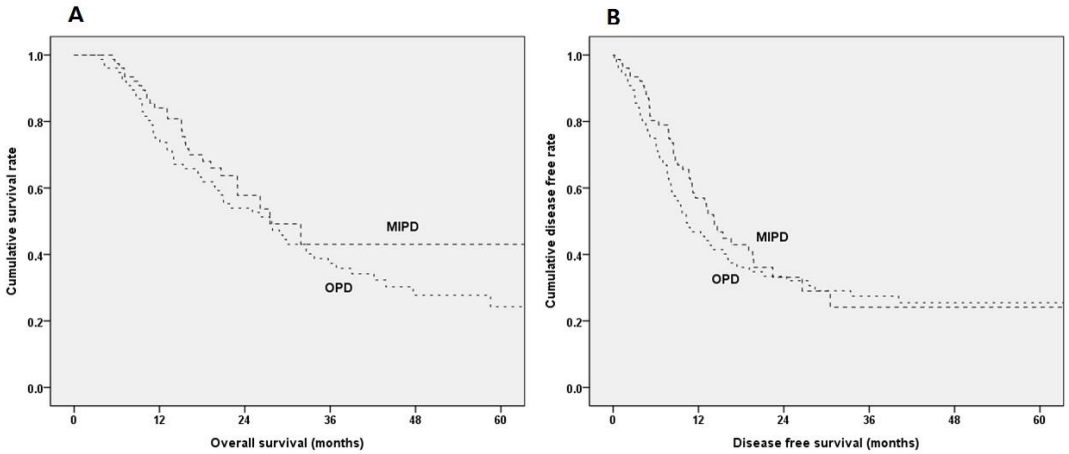

Figure 7. Kaplan-Meier survival curves of MIPD group (n=76) and OPD group (n=76) after propensity score matching. (A) The median OS and estimated 1-, 2-, and 5-year OS were respectively 27.5 months, 84.1%, 57.8%, and 43.0% in MIPD group and 24.5 months, 75.0%, 53.9%, and 24.3% in OPD group (p = 0.257). (B) The median DFS and estimated 1-, 2-, and 5-year DFS were respectively 14.2 months, 57.0%, 33.1%, and 24.1% in MIPD group and 10.3 months, 46.8%, 33.4%, and 25.5% in ODP group (p = 0.402).

서론(Introduction)

Minimally invasive surgery (MIS) has become the standard of care for many surgical procedures across different specialties. Currently, it is the standard procedure for the resection of intraabdominal organs, including the stomach[1, 2], gallbladder[3], spleen[4, 5], colon[6, 7], and kidney[8, 9]. However, it finds limited use in pancreatic surgery because of the complexity of these operations. MIS for benign and malignant pancreatic disease has recently become widely accepted and is attracting research attention[10-12]. However, minimally invasive pancreatectomy (MIP) still has the limitation of generalizability, and open surgery is still widely practiced for pancreatic ductal adenocarcinoma (PDAC) because of concerns about adequate oncological outcomes and the potential for significant perioperative complications. Recently, studies on laparoscopic distal pancreatectomy (LDP) for left-sided PDAC have been published in several institutions including ours[10, 13, 14]. Studies have also reported on laparoscopic pancreaticoduodenectomy (LPD) for PDAC, which is located at the head of the pancreas, and uncinate processes[12, 15]. However,

indications of MIP for PDAC with open pancreatectomy (OP) were still different depending on sex, body mass index (BMI), American Society of Anesthesiologists (ASA) score, resection of major vessels or other organs, and neoadjuvant chemotherapy. There is still a lack of data on the perioperative and oncologic outcomes after MIP for PDAC. Our institution, the Asan Medical Center, Seoul, South Korea, is a leading tertiary care institution in South Korea. It has extensive experience with laparoscopic pancreatic surgery[13, 16, 17], which is preferred to LDP or robot distal pancreatectomy (RDP) for left-sided PDAC, and we have also performed selective LPD and robot pancreaticoduodenectomy (RPD) for PDAC located at the head of the pancreas. At this time, it is meaningful to identify the indication, postoperative outcome, and oncological outcome of MIP for PDAC currently performed by our institution.

This study aimed to compare demographics, perioperative outcomes, and oncologic outcomes between the currently performed MIP and OP for PDAC at Asan Medical Center.

연구 방법 (Materials and methods)

1. Patient database

Between January 2011 and December 2017, a total of 5126 consecutive patients underwent pancreatectomy at Asan Medical Center. The inclusion criteria were patients treated with distal pancreatectomy or pancreaticoduodenectomy for PDAC. Both MIP and OP were included in the study. MIP was defined in this study as LDP, RDP, LPD, and RPD. Minimally invasive distal pancreatectomy (MIDP) included LDP and RDP, and minimally invasive pancreaticoduodenectomy (MIPD) included LPD and RPD. Patients who had benign lesions or periampullary malignancy except PDAC were excluded in this study. Patients who had other kinds of pancreatic cancer (e.g., acinar carcinoma, endocrine tumor, or mucinous carcinoma) were also excluded from this study. Total pancreatectomy or central pancreatectomy for PDAC cases were excluded because the number of cases was small. Based on these inclusion and exclusion criteria, 1162 patients were enrolled in this study. These patients were classified into two groups: distal pancreatectomy and

pancreaticoduodenectomy. Each group was subdivided into groups with minimally invasive surgery and open surgery (Figure 1). Data on selected patients were obtained from the electronic medical records of our institute and were reviewed retrospectively. The following clinicopathological data were collected and investigated: age, sex, BMI, ASA physical status classification, CA 19-9, modified Glasgow Prognostic Score (mGPS)[18], operative procedure, concurrent vessel resection, concurrent resection of other organs, neoadjuvant chemotherapy, operative time, pathologic finding, tumor size, TNM stage (American Joint Committee on Cancer stage 8th edition), postoperative pancreatic fistula (POPF), postoperative complication, and adjuvant chemotherapy. In pathologic findings, the resection margin status was categorized as R0 or R1. If the closest safe resection margin was less than 1 mm, it was categorized as R1. POPF was graded according to the definition updated in 2016 by the International Study Group Pancreatic Fistula[19], and postoperative complications were classified according to the Clavien-Dindo classification[20]. Follow-up data were also obtained from electronic medical records. For postoperative surveillance in

all patients, contrast-enhanced abdominoperineal CT was used, and CA 19-9 levels were examined every 3 months for the first 2 years following surgery and then every 6 months. Recurrence was diagnosed based on detecting new progressive lesions and elevated CA 19-9 levels. When lesions of potential recurrent disease were detected, ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) and/or chest CT were performed, and a biopsy was performed to confirm the diagnosis of recurrence if differential diagnosis was needed. The duration of overall survival (OS) was measured from the time of surgery until death or the last visit to the outpatient department.

2. **Surgical technique**

a. Laparoscopic distal pancreatectomy

LDP was performed in a reverse Trendelenburg position with the table tilted toward the right side, so that the left side was tilted upward by around 15°–20°. Four ports (two 12 mm and two 5 mm) were used for LDP. The lesser sac was entered by dividing the gastrocolic ligament. The stomach was retracted upward by a stay suture placed in its posterior wall and

was pulled outside the abdomen via endoclose. Then, the spleen was mobilized from the splenic flexure and proximal descending colon. Next, tunneling was performed under the pancreas by dissection on the inferior border of the pancreas over the superior mesenteric vein (SMV) until the pancreas mobilized completely from the SMV/portal vein (PV). Then, the pancreas is encircled with umbilical tape to facilitate stapler insertion and pancreas transection line. Pancreas transection was performed slowly using a linear stapler over 3 min to minimize parenchyma laceration and well control bleeding. Dissection of the lower border of the pancreas from the retroperitonium was performed from the medial to the lateral sides. The splenic artery was dissected from the upper border of the pancreas. The splenic artery and vein are encircled and divided between locking clips. For combined splenectomy, dissection continued up to the gastrosplenic ligament including the short gastric vessels using an energy device and clips. Pancreas dissection from the retroperitonium continued until the splenic hilum. Finally, the spleen was mobilized to finish the procedure. PDAC patients underwent LDP based on the concept of anterior or

posterior radical antegrade modular pancreatosplenectomy (RAMPS), in which the peripancreatic retroperitoneal tissue (anterior RAMPS), along with the perinephric and adrenal (posterior RAMPS) tissue, are taken en bloc. If PDAC invaded the celiac axis, celiac axis resection was also performed during the operation.

b. Robot distal pancreatectomy

We used the da Vinci Robotic Surgical System (Si or Xi model, Intuitive Surgery) for all our RDP cases. The surgical procedure of RDP is similar to that of LDP. RDP was performed in the same position as LDP using 3 robotic trocars including a 12-mm camera port and a 12-mm accessory port for the assistant. After the stomach was retracted by the assistant by the same method as that in LDP, the robot was docked into position. After the lesser sac was opened through the greater omentum, the distal pancreas and splenic hilum were fully visualized using the robot energy device. After tunneling under the pancreas via dissection on the inferior border of the pancreas, pancreas transection was performed using the linear stapler that is inserted through the 12-mm accessory port. The subsequent procedure is the

same as the surgical procedure for LDP.

c. Open distal pancreatectomy (ODP)

The patient was placed in a supine position. The operation usually required a long midline incision or inverted L incision. The surgical procedure was the same as that for LDP.

d. Laparoscopic pancreaticoduodenectomy

The patient was placed in a supine position. An anti-Trendelenburg (10°–30°) was used to expose the operation field. Two monitors were placed on both sides of the patient. The operator and laparoscopist stood to the right of the patient, with the first assistant positioned to the left. The operator's right-hand port (12 mm) was inserted through the left side of the umbilicus. A further four trocars were placed. Figure 2 shows the trocar locations. After abdominal access was established, the greater omentum was divided using the energy device. The right colon was fully mobilized from the liver and duodenum. The retropancreatic SMV was exposed and the right gastroepiploic vessels were transected. After removing soft tissue around the SMV and superior mesenteric artery, each vessel was

hung with a vessel loop. The mobilization of the duodenum to the Treitz ligament was performed with traction of the duodenum toward the opposite side by the assistant surgeon. The stomach or duodenum was divided using an endoscopic linear stapler. After cholecystectomy, dissection of the hepatoduodenal ligament and isolation of the common bile duct were performed. After identifying the right and the left hepatic artery, lymph node dissection was performed. The gastrohepatic ligament was opened to visualize the superior border of the pancreas, and the common hepatic artery was identified. The right gastric artery and gastroduodenal artery were identified and transected using a Hem-o-lok clip. The pancreas was divided above the SMV using the energy device. After retracting the resected pancreas toward the right side of the patient, the portal vein was identified and hung with a vessel loop. The jejunum was divided 10–15 cm distal to the Treitz ligament using an endoscopic linear stapler. The energy device and endoscopic electrocautery were used to divide the remnant soft tissue and branches from the superior mesenteric artery between the uncinate process of the pancreas and the superior mesenteric artery to complete resection.

Pancreaticojejunostomy was performed using the double layered, end-to-side duct-to-mucosa method using a laparoscopic suture. A polyethylene internal stent was inserted in the pancreatic duct. End-to-side choledochojejunostomy was performed using laparoscopic continuous suturing of the posterior wall and interrupt or continuous suturing of the anterior wall. Duodenojejunostomy or gastrojejunostomy with jejunojejunostomy were performed extracorporeally using the specimen extraction site, namely, the umbilicus port place after extension. Closed duction drains were placed at the superior and inferior border of the pancreaticojejunostomy site.

e. Robot pancreaticoduodenectomy

The patient position was the same as that in LPD. The surgeon's positions were also the same as those for LPD. RPD is divided into two major surgical procedures. First, resection was performed using a laparoscopic instrument in the same way as in LPD, and then, duct-to-mucosa pancreaticojejunostomy and end-to-side choledochojejunostomy were performed using a robot device. The location of the trocar was the same as that in LPD. The operator's

two ports and the assistant port were replaced with a robotic 8-mm port for inserting the robotic arm. Second, there is a method for performing pancreaticoduodenectomy using a robotic device for resection. Four robotic trocars including a 12-mm camera port and two accessory ports for the assistant were used in the operation (Figure 2). The operation procedure was the same as that in LPD except that the robot arm was used. After choledochojejunostomy, the specimen was extracted through the extended robot camera port site. Duodenojejunostomy or gastrojejunostomy with jejunojejunostomy were also performed extracorporeally.

f. Open pancreaticoduodenectomy (OPD)

The patient was placed in a supine position. The operation usually required a long midline incision or inverted L incision. The surgical procedure was the same as that in LPD.

3. Comparative analysis

Demographics, perioperative outcomes, pathologic outcomes, and oncologic outcomes of each MIDP versus ODP and MIPD versus OPD groups were compared. Statistical analyses were performed using SPSS 21.0 (IBM Corp., Armonk, NY, USA). Continuous variables were reported as the mean, median, and range whenever appropriate, and the variables were compared using Student's t test. Categorical variables were compared using the chi-square test, Fisher's exact test, or linear-by-linear association test. All tests were two-sided, and p value ≤ 0.05 was considered significant. Survival curves were generated using the Kaplan-Meier method. The comparison of survival according to each MIP and OP was performed using the log rank test. Propensity score-matching (PSM) analysis between MIDP and ODP were also performed in this study. PSM analysis reduced the impact of treatment-selection bias on the estimation of causal treatment effects when using a retrospective cohort study. To estimate the propensity score, a logistic regression model using seven covariates was performed for analyzing DP and PD. Two continuous variables including Age and BMI, and five categorical variables including sex (male or female), ASA score (grade I to III), CA 19-

9 range (normal, increased [>37 U/mL]), mGPS (0, 1or 2), and concurrent resection of other organ (yes or no) were included for analyzing DP patients. For PSM of PD, other independent factor were same with DP except concurrent resection of other organ. In PSM of PD patients, concurrent resection of other organ was replaced by neoadjuvant chemotherapy. Because of the small number of neoadjuvant chemotherapy and concurrent vessel resection patients who underwent MIDP, PSM was not corrected, and therefore, the data were excluded from both ODP and MIDP in PSM analysis. This matching was performed using a caliper width of 0.1 standard deviations of the logit of the estimated propensity score. After PSM, two matched groups were handled as unpaired independent groups. To estimate the prognostic effects of MIP, multivariate logistic regression, Kaplan-Meier survival curve, and log rank test were performed for OS and disease-free survival (DFS).

결과 (Results)

Chaptor 1. Distal pancreatectomy

1. Demographics

Based on the inclusion and exclusion criteria, 1162 patients were found to be treated by pancreatectomy for PDAC. Table 1 shows the demographics for the 363 patients (203 male, 160 female) after DP. Among them, 184 patients underwent MIDP (including seven cases of RDP), 179 patients underwent ODP. The mean age of the included patients was 63.0 (range 30.0–88.0). BMI, ASA score, proportion of elevated CEA, concurrent resection of other organs were not different between MIDP and ODP. More patients in the ODP group received neoadjuvant chemotherapy when compared to the MIDP group (14.0% vs 1.6%, $p < 0.001$). Concurrent vessel resection was also performed more in the ODP group (18.4% vs 2.2%, $p < 0.001$).

2. Perioperative outcomes

Table 2 shows the perioperative outcomes of distal pancreatectomy. The operative time of MIDP was shorter than that of ODP (210 min vs 236 min, $p < 0.001$). The postoperative hospital stay was shorter in MIDP than in ODP (8 days vs 11 days, $p < 0.001$). The incidence of POPF and surgical complications were not different between the MIDP and the ODP groups. The distribution of patients receiving adjuvant treatment did not differ between MIDP and ODP.

3. Pathologic outcomes

Table 2 also shows the pathologic outcomes after the operation. Tumor size, TNM stage (American Joint Committee on Cancer stage 8th edition), differentiation, perineural invasion, positive lymph node, and resection margin were not different between MIDP and ODP. The proportion of lymphovascular invasion was greater in the ODP group than in the MIDP group (53.6% vs 39.7%, $p = 0.009$). The number of harvest lymph nodes was larger in the ODP group than in the MIDP group (16.0 vs 14.0, $p = 0.037$); however, the lymph

node ratio was not different between the two groups.

4. Survival outcome

The median follow-up period was 29 months (range, 1–90 months). Figure 3 shows Kaplan-Meier survival curves of OS and DFS in patients who underwent MIDP and ODP. The median OS following surgery was respectively 32.6 and 25.0 months in the MIDP and ODP groups. OS without correction was better in the MIDP group than in the ODP group (p-value = 0.023). The median DFS was respectively 13.3 and 10.4 months in the MIDP and ODP groups. PFS without correction was better in the MIDP group than in the ODP group (p-value = 0.020). Figure 4 shows subgroup analysis of the Kaplan-Meier survival curves between MIDP and ODP according to AJCC 8^{th} stage. The median OS was respectively 84.0 and 42.4 months in the stage I MIDP (n = 65) and ODP groups (n = 51). OS was not significantly different between the two groups (p = 0.283). Stage II was not significantly different between the MIDP (n = 80) and ODP groups (n = 87) for OS (23.3 months vs 22.0

months; p = 0.101). There was also no significant difference between the stage III MIDP (n = 39) and ODP groups (n = 41). The median OS was respectively 23.0 and 22.1 months in the MIDP and ODP groups (p = 0.394).

5. Propensity score match for distal pancreatectomy

After PSM, 118 patients of the MIDP group were matched to 118 patients of the ODP group. Table 3 shows demographics after PSM and Table 4 shows perioperative outcome about DP after PSM. The result was not different with non-corrected data. Operation time (204 min vs 224 min, p = 0.029) and hospital stay after operation (8.5 days vs 10.5 days, p < 0.001) were shorter in MIDP patients. Number of harvested lymph node was not different between two group after PSM, but the proportion of lymphovascular invasion was greater in the ODP group than in the MIDP group (55.9% vs 38.1%, p = 0.009). Table 5 shows hazard ratio of propensity score matching and propensity score inverse probability of treatment weight (IPTW) analysis. In multivariate, PSM, and PS-IPTW analysis, the MIDP group showed

better OS and DFS than the ODP group <Multivariate : OS HR = 1.44 (p = 0.014), DFS HR = 1.46 (p = 0.008), ; PSM : OS HR = 1.20 (p = 0.256), DFS HR = 1.26 (p = 0.126) ; Propensity score IPTW OS HR = 1.43 (p <0.001), DFS HR = 1.44 (p<0.001)>. PSM showed a boundary difference, whereas multivariate and IPTW analysis showed a statistically significant difference between the MIDP and ODP groups. Figure 5 shows Kaplan-Meier survival curves of the MIDP (n = 118) and ODP groups (n = 118) after PSM.

Chaptor 2. Pancreaticoduodenectomy

1. Demographics

Table 7 shows the demographics for the 799 patients(487 male, 312 female) after PD. Among them, 76 patients underwent MIPD (including 11 cases of RPD), and 723 patients underwent OPD. The mean age of the included patients was 61.6 (range 32.0–85.0). Age, sex, BMI, ASA score, proportion of elevated CEA, the proportion of preoperative biliary drainage methods, neoadjuvant chemotherapy concurrent resection of other organs were not

different between MIPD and OPD. The proportion of increased CA19-9 (66.5% vs 50.0%, p = 0.013) and concurrent vessel resection (37.3% vs 15.8%, p < 0.001) were higher in OPD than MIPD.

2. Perioperative outcomes

Table 8 shows the perioperative outcomes of PD. The operation time of MIPD and OPD were not different statistically (392 min vs 385 min, p = 0.578). The postoperative hospital stay for MIPD patients was also shorter than that for OPD patients (10 days vs 13 days, p < 0.001). The incidence of POPF and surgical complications were not different between the MIPD and the OPD groups. More patients in MIPD received adjuvant treatments than in OPD (80.3% vs 67.1%, p = 0.047).

3. Pathologic outcomes

Table 9 shows the pathologic results of MIPD versus OPD. The pathologic tumor size was

smaller in the MIPD group (2.7cm vs 3.1cm, p = 0.008), and therefore, the proportion of T stage was different between the MIPD and OPD groups. The proportion of perineural invasion was larger in the OPD group than in the MIPD group (69.7% vs 90.0%, p = 0.001). The number of harvest lymph nodes and positive lymph nodes were higher in the OPD group; however, the lymph node ratio was not different between the two groups. Other factors were not different between the MIPD and OPD groups.

4. Survival outcome

Figure 6 shows Kaplan-Meier survival curves of the MIPD (n = 76) and OPD groups (n = 723). The median OS was not different between the two groups (27.5 months vs 23.8 months, p = 0.104); however, DFS was different in unmatched analysis. DFS was better in the MIPD group than in the OPD group (14.2 months vs 10.2 months, p = 0.031).

5. Propensity score match for distal pancreatectomy

After PSM, 76 patients of the MIPD group were matched to 76 patients of the OPD group. Table 8 shows demographics after PSM and Table 9 shows perioperative outcome about PD after PSM. Hospital stay after operation was shorter in MIPD before correction, but after PSM, this result was not different statistically (12.3 days vs 14.0 days, p=0.063). The difference in tumor size, T stage, perineural invasion, number of harvested lymph node, number of positive lymph node between MIPD and OPD were not different after using PSM analysis.

Table 10 shows hazard ratio of propensity score matching and propensity score inverse probability of treatment weight (IPTW) analysis. In multivariate, PSM, and PS-IPTW analysis, OS and DFS were not different between MIPD and OPD. <Multivariate : OS HR = 1.37(p = 0.110), DFS HR = 1.35 (p = 0.052), ; PSM : OS HR = 1.30 (p = 0.257), DFS HR = 1.36 (p = 0.405) ; Propensity score IPTW OS HR = 1.35 (p=0.095), DFS HR = 1.35 (p=0.036)>. Figure 5 shows Kaplan-Meier survival curves of the MIPD (n = 76) and OPD groups (n = 76) after PSM.

고찰（Discussion)

Chaptor 1. Distal pancreatectomy

PDAC is one of the leading causes of death worldwide. Effective treatment of PDAC has remained a challenge in the fields of medicine and surgery. Because surgical resection for PDAC can be associated with high morbidity and eventual recurrence, a multimodal approach to PDAC treatment is encouraged to maximize the quality and quantity of life. Several studies have reported that MIDP showed better surgical outcomes than ODP for PDAC. However, the indications of MIDP are still limited. Shin et al.[13] reported that LDP was safer and more efficacious than ODP after propensity score adjustment for presurgical variables of return to diet and length of stay based on our institutional data for 2015. These data were collected from 2006 to 2013, and BMI and tumor size were different between LDP and ODP patients in this report. Furthermore, the tumor location and concurrent resection of other organs were different between LDP and ODP in a pan-European propensity-score-matched study[14]. Over time, the indications for MIDP have gradually

expanded, and our current study did not show differences in BMI, tumor size, and resection of other organs. In our study, the proportion of concurrent vessel resection and neoadjuvant patients were smaller in MIDP patients. Laparoscopic vessel resection and anastomosis during pancreatectomy have just begun and have been reported[21]. We also performed four cases of vessel resection with anastomosis during MIDP until 2016; the number of such cases is continuing to increase. Neoadjuvant chemotherapy with FOLFIRINOX (fluorouracil, leucovorin, irinotecan, and oxaliplatin) has been started in our institution since 2013[22]. The indication of MIS for PDAC after neoadjuvant chemotherapy has also increased since then. These two factors may influence perioperative and oncological outcomes; however, patients in need of such treatment are also increasingly becoming indications for MIDP. If we could overcome the weaknesses of MIDP, we could perform a randomized control trial of MIDP and ODP.

In our study, the MIDP operation time was shorter than that of ODP. Several studies have reported that the operation time of LDP is comparable or shorter than that of ODP[23, 24].

These results suggest that as surgeons' experience of MIDP increases, its operation time will reduce as surgical technique develop. POPF, postoperative complications, and 90 days in hospital mortality were not different between the two groups. These results have also been reported by many other studies[13, 14, 25], and they verify the feasibility of MIDP.

Table 3 shows that there were no pathologic differences between MIDP and ODP except for lymphovascular invasion and number of harvested lymph nodes. A study reported that in LDP, smaller lymph nodes were harvested and they showed lower proportion of lymphovascular invasion than in the case of ODP[14]. Although RAMPS and vessel resection within MIDP are increasing, more studies are needed on the difference between harvested lymph nodes and lymphovascular invasion.

An unmatched analysis indicated that MIDP showed better OS and PFS than ODP in this study. In addition, when PSM and inverse probability of treatment weight analysis were performed, MIDP showed better survival than ODP. Because neoadjuvant chemotherapy and vessel resection were not corrected for PSM, this can be interpreted as a comparison of

postoperative survival for resectable PDAC, but not including borderline resectable PDAC. Recently, some retrospective studies have reported that laparoscopic distal pancreatectomy for PDAC had similar oncologic outcomes[13, 14, 23]. Kanto et al.[26] reported that LDP showed comparable oncologic outcomes with ODP without PSM analysis. Ricci et al.[25] reported that a laparoscopic approach did not affect the overall survival rate. The survival benefit of MIDP in our study could be because its surgical resection range is comparable to that of ODP for resectable PDAC with short operation time, and it has shortened duration of hospitalization. Although there was no significant difference in survival in each stage, when we saw the same tendency in all three stages, we could interpret this as a result of the number of patients per stage being reduced. The PSM and propensity score IPTW analysis also implies that MIDP has a better survival rate than ODP for resectable PDAC. A randomized control trial will ultimately clarify the survival benefit of MIDP. However, the current study itself indicates that MIDP will have a better survival rate than ODP for resectable PDAC.

Chaptor 2. Pancreaticoduodenectomy

MIPD was developed from Gagner and Pomp's first description of LPD in 1994[27]. Several studies have reported that LPD might not only be feasible but also afford advantages compared with OPD for benign and periampullary malignancy[28-30]. However, MIPD for PDAC has yet to show limitations of indications because of the intimate relationship with major surrounding structures, inflammatory change around the head of the pancreas, and invasion of major vessels. Stauffer et al. reported that 24.1% of LPD cases converted to OPD cases due to vein resection or adherence to the underlying vasculature resulting from pancreatitis/desmoplastic reaction[15]. Demographic data was different between the MIPD and OPD groups in our study. The difference of CA19-9, mGPS, and concurrent vessel resection means that MIPD is being performed in patients with less inflammatory and less aggressive tumors. Perioperative outcomes showed that there was no difference in operation time, and the duration of hospitalization after operation was shorter in MIPD than in OPD. Our institution and other studies have reported that MIPD requires

longer operation time than OPD[15, 17, 28, 31]. In the current study, there was no statistically significant difference in operation time, although it was still long. This result suggests that as with MIDP, experience accumulates, and accordingly, the operation time reduces. Vessel resection during MIPD still remained the main problem because of the difficulty of performing this procedure and the complications caused if the procedure failed. However, many studies have reported on the efforts required for and the results obtained by performing this surgery[32, 33]. In our study, 11 cases of MIPD (14.5%) were performed with superior mesenteric vein or portal vein resection with end-to-end anastomosis. The stability should be studied further; nonetheless, the indications are gradually increasing. The results of shorter postoperative hospital stay than in the case of OPD, no difference in POPF, complication rate, and mortality were the same as in other studies. Adjuvant treatment was performed more frequently in patients undergoing MIPD even if the pathologic outcome was different between MIPD and OPD. No study has reported on the relationship between MIP and adjuvant therapy. Several studies have reported on colorectal cancer surgery;

however, it is unclear whether MIS is beneficial for adjuvant therapy[34, 35]. Although short hospital stay and low postoperative pain may have an impact, this seems to require more research. The tumor size, T stage, perineural invasion, number of harvested lymph nodes, and number of positive lymph nodes were different between MIPD and OPD. These results indicate that the patient is selected when planning MIPD. A low number of harvested lymph nodes and positive lymph nodes also means that it is difficult to remove lymph nodes during MIPD. However, the TNM stage and R0 resection were not different between the two groups. Furthermore, the perioperative outcome and pathologic outcome were not different after PSM analysis. This result could mean that the results of MIPD-selective patients may be similar to that of OPD. DFS was better in MIPD than in OPD (14.2 months vs 10.2 months, $p = 0.031$) before correction, but OS and DFS were not different between MIPD and OPD after PSM. It cannot support the suggestion that MIPD can have a similar oncologic result to OPD for all of PDAC patients, but we can insist that MIPD in selected patients can yield postoperative and oncologic results as OPD.

The current study has some limitations. Data were collected retrospectively and MIPD cases were still not enough compared to OPD cases. There might be inherent selection bias as patients who are determined to be candidates for MIP are likely more favorable from the viewpoint of vessel invasion of tumor and neoadjuvant chemotherapy. Because we did not calibrate all demographic data for each group, we cannot assert that the results are highly reliable, and the results may also be statistically biased. Nevertheless, this study notes that as increasing experience is gained for MIP, its indications are becoming increasingly similar to those of OP. The perioperative outcomes of MIP have also improved, such as reduced operating time for both MIDP and MIPD. The pathologic and oncologic outcomes of MIDP are also comparable to those of ODP in the present study. MIDP shows better survival than ODP for resectable PDAC. MIPD is feasible, can be performed safely and survival was also comparable to OPD in selected patients.

결론（Conclusion)

There is still a tendency to choose patients suitable for MIP; however, the indications are increasing. The operation time was shorter in MIDP than in ODP, and postoperative hospital stay was shorter in MIP than in OP. The pathologic outcomes and survival after operation of MIDP were comparable to those of ODP for PDAC, and MIDP shows better survival for resectable PDAC. MIPD is feasible, can be performed safely and survival was also comparable to OPD in selected patients.

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국문요약

대규모 단일 기관에서 시행된 췌장선암에 대한 최소침습췌장절제술 대 개방췌장절제술의 비교

서론 : 췌장선암에 대한 치료는 적절한 종양학 결과 및 수술 전후 합병증에 대한 우려로 최소 침습성 췌장 절제술은 여전히 일반화 가능성의 한계를 지니고 있으며. 아직까지 개복 췌장 절제술을 선호하고 있다. 이러한 이유로 췌장선암에 대한 췌소침습췌장절제술의 수술 전, 후 결과 및 종양 학적 결과에 대한 보고는 아직까지 부족하다. 이 시점에서 현재의 최소침습췌장절제술과 개복을 통한 췌장절제술 간의 적응증의 차이 및 수술 전, 후 결과, 종양학적 결과에 차이가 있는지 확인하는 것은 의미가 있다.

연구 대상 및 방법 : 이 연구는 2011년 1 월부터 2017년 12월까지 서울 아산

병원에서 췌장선암으로 수술은 받은 1162명의 환자를 대상으로 하였다. 최소침습췌미부절제술(MIDP) 대 개복췌미부절제술(ODP) 및 최소침습췌두십이지장(MIPD) 절제술 대 개복췌두십이지장 절제술(OPD)을 받은 환자의 인구학적 데이터, 수술 전, 후 결과, 병리학적 결과 및 생존률을 후향적으로 검토하고 비교하였다.

결과 : 우선 184 명의 MIDP 환자를 179 명의 ODP 환자와 비교하였다. MIDP 환자 군이 ODP 환자군에 비해 신보강화학요법(1.6% vs 14.0%, p<0.001) 및 동시혈관절제술을 받은 비율이 더 적었다(2.1% vs 18.4%, p<0.001). MIDP 는 ODP 에 비해 더 짧은 수술 시간 (210 vs 236 min, p<0.001) 과 수술 후 재원기간 (8 vs 11 days, p<0.001) 을 보였다. 그 이외 다른 수술 전, 후 결과는 차이가 없었다. MIDP 와 ODP 간의 병리학적 결과는 lymphovasucular invasion (39.7% vs 53.6%, p=0.009) 과 harvested lymph node (14.0 vs 16.0, p=0.037) 이외에는 다른 결과에서는 차이를 보이지 않았다. MIDP는 성향점수매칭 (HR =

1.20, p = 0.256)과 역확률가중치모형(HR = 1.43, p = 0.001)에서도 ODP보다 더 나은 생존율을 보였다.

다음으로 76 명의 MIPD 환자와 723 명의 OPD 환자를 비교했다. MIPD 환자군은 OPD 환자군에 비해 상승된 CA19-9 비율(50% vs 66.5%, p=0.013), mGPS 의 분포(p=0.016), 동시혈관절제술의 비율(15.8% vs 37.3%, p<0.001)이 더 적었다. MIPD 는 OPD 에 비해 더 짧은 재원 기간을 보였다 (10 vs 13 days, p<0.001). ; 그 이외 다른 수술 전, 후 결과는 차이가 없었다. MIPD와 OPD는 T stage, 종양 크기, 수확 및 양성 림프절 수에 차이가 있었고 그 이외에 병리학적 결과는 차이가 없었다. 성향점수매칭 이후 MIPD 와 OPD 간의 수술 전후 결과 및 병리학적 차이는 없었다. 성향점수매칭 이후 MIPD와 OPD의 생존율 또한 같았다.

결론 : 아직 까지 최소침습췌장절제술에 적합한 환자를 선택하는 경향은 있으나 적응증은 확대되고 있다. MIDP는 ODP보다 수술 시간이 짧았고 MIP는 개복 수

술보다 수술 후 입원 기간이 짧았다. MIDP는 ODP와 비교하였을 때 유사한 병리학 적 결과를 보였으며 절제 가능한 PDAC에 대해서는 더 나은 생존율을 보였다. MIPD는 안전하게 시행되어 질 수 있고 선택적인 환자에게서는 수술 후 생존율이 OPD 와 같다고 할 수 있다.