Surgical and survival outcomes after robotic and open pancreaticoduodenectomy with positive margins

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Abstract

Background: Though nowadays a palliative pancreaticoduodenectomy (PD) can be performed safely with relatively low mortality and acceptable morbidity rates in experienced centers, there have been no studies on the routine use of a palliative PD or on the advantages of performing surgical resection as a debulking procedure. Furthermore, the impact of resection margins on survival outcomes has been a matter of controversy. Therefore, this study aimed to clarify the role of robotic PD (RPD) in pancreatic and periampullary adenocarcinomas with positive resection margins.

Methods: Patients undergoing RPDs and open PDs (OPDs) were included in this study. Based on the resection margins, the patients were divided into the R0, R1, and R2 PD groups. Surgical risks and survival outcomes were analyzed.

Results: There were 348 PDs, including 29 (8.3%) palliative and 319 (91.7%) curative. Primary tumor origin, tumor sizes, perineural invasions, and abnormal serum carcinoembryonic antigen (CEA) levels were factors leading to palliative resection. The multivariate analysis showed that only pancreatic head adenocarcinomas and abnormal serum CEA levels (>5 ng/mL) were independent predictors. The surgical risks between curative and palliative PD were similar. There were no significant differences in the surgical risks and other surgical parameters between palliative RPDs and OPDs. For curative resection, RPDs resulted in less blood loss, greater harvested lymph nodes yield, less postoperative complications, less delayed gastric emptying, and shorter hospital stays than OPDs. The survival outcome was significantly better following R0 resection in overall periampullary adenocarcinomas, whereas a significant survival difference was shown only between the R0 and R2 resections for pancreatic head adenocarcinomas.

Conclusion: Compared with R0 PDs, palliative R1 PDs could benefit patients with pancreatic head adenocarcinomas when considering survival outcomes without increasing surgical risks. RPD can be considered for curative purposes and as an alternative for palliative management.

Keywords: Palliative; Pancreatic; Pancreaticoduodenectomy; Periampullary; Robotic

1. INTRODUCTION

The only type of curative treatment for pancreatic and periampullary cancers is a pancreaticoduodenectomy (PD).[1,2] A complete tumor resection with negative margins has been regarded as an essential prerequisite for favorable survival outcomes and the primary goal of surgical treatment for these malignant diseases.[3–6] However, reliance on only preoperative evaluations or even intraoperative findings has limited the accuracy of predicting the possibility of curative pancreatic and periampullary resections. To achieve an extensive surgical exploration, an aggressive surgeon with sufficient ability usually performed the operation to the "point of no return" and then ultimately proceeded to complete the PD, though it may have resulted, finally, in a palliative resection.[7]

Though nowadays a palliative PD can be performed safely with relatively low mortality and acceptable morbidity rates in experienced centers,[3,7,8] there have been no studies on the routine use of a palliative PD or on the advantages of performing surgical resection as a debulking procedure.[9] Furthermore, the impact of resection margins on survival outcomes has been a matter of controversy.[6] Some studies have reported that a positive margin of resection was an independent predictor of a poor outcome following PDs for a pancreatic adenocarcinoma,[5,6,10–13] while paradoxically, other studies have demonstrated that PDs with a positive margin may improve survival and quality of life; however, this may not be related to an increase in perioperative morbidity and mortality, when compared with surgical bypasses.[3,7,8,14–17]

In light of the aforementioned findings and gaps in the literature, this study aimed to determine the predictors of resection margin status in pancreatic and periampullary adenocarcinomas and to provide the incidence of palliative resection with a positive margin after robotic PD (RPD) and open PD (OPD). We investigated the role of palliative PDs by comparing the surgical

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risks and survival outcomes between the robotic and traditional open approaches. Furthermore, we aimed to clarify the impact of a 1-mm surgical margin on survival in a pancreatic head adenocarcinoma.

2. METHODS

Data on patients with periampullary adenocarcinoma who underwent PD between July 2012 and June 2019 were retrieved for this retrospective study from a computer database with prospectively collected data. This study was approved by the Institutional Review Board (TPEVGH IRB NO.: 2019-11-001AC). Patients with surgical mortality were not included in the survival analysis. Surgical mortality was defined as perioperative death within the first 90 days following surgery.

The surgical approach was either RPD or OPD. All the RPD and OPD procedures were performed by the same team using the same technique of pancreatic reconstruction with modified Blumgart pancreaticojejunostomy.[18,19]

Resection was stratified into three categories based on the resection margin status: R0, resection without both gross and microscopic evidence of cancer at the resection margin, with the definition of margin being >0 mm instead of 1 mm as defined by the National Comprehensive Cancer Network; R1, resection with grossly negative but microscopically positive cancer evidence at the resection margin; and R2, resection with grossly positive cancer evidence at the resection margin.[20] In this study, R0 was considered to be a curative PD, whereas both R1 and R2 were considered to be palliative PDs. The resection margins for evaluation included the pancreatic neck, uncinate process along the superior mesenteric vein, retropancreatic margin, and bile duct.

The demographics, intraoperative variables, surgical risks including surgical morbidity and mortality, and oncologic outcomes such as the radicality and yield of harvested lymph nodes were compared between the palliative PD and curative PD groups. The survival outcomes were compared among the R0, R1, and R2 PD groups. The impact of the 1-mm margin on the survival outcome was also evaluated in the R0 PD group.

The clinically relevant pancreatic leakage included grade B or C postoperative pancreatic fistulas (POPFs) according to the definition from the 2016 update of the International Study group of Pancreatic fistula.[21] Postpancreatectomy hemorrhage (PPH) and chyle leakage after pancreatic operations were defined based on the consensus of the International Study Group of Pancreatic Surgery (ISGPS);[22,23] gastric atonia—also defined on the basis of the consensus of the ISGPS—included grade B or C delayed gastric emptying (DGE) after pancreatic surgery.[22]

The statistical analysis was performed using Statistical Product and Service Solutions (SPSS) version 21.0 software (SPSS Inc.; IBM, Armonk, NY). All continuous data were calculated using the means ± SDs or medians and frequencies as appropriate for the type of data being analyzed. Categorical variables were compared using the χ^2 test or Fisher's exact test. A binary logistic regression model was used in the multivariate analysis to determine the independent predictors of resection status. Actuarial survival rates were estimated using the Kaplan–Meier method. The log-rank test was used to compare the differences in the survival curves. For all the analyses, $p < 0.05$ was considered statistically significant.

3. RESULTS

There were 348 patients with periampullary adenocarcinoma who underwent PD, including 29 (8.3%) palliative PDs (R1 and R2) and 319 (91.7%) curative PDs (R0). The risk factors for palliative resections are listed in Table 1. Type of operation approach (177 [50.9%] RPD vs 171 [49.1%] OPD), sex, age, additional vascular resections, chemotherapy, tumor cell differentiation, lymph node involvement, lymphovascular invasions, and abnormal serum CA 19-9 levels >37 U/mL were not predictors of palliative resections in periampullary adenocarcinomas. Pancreatic head adenocarcinoma was the main primary tumor of origin. It also accounted for a higher incidence in the palliative PD group (86.2%) than in the curative PD group (48.0%) ($p < 0.001$). A tumor size >2 cm was noted in 27 (93.1%) cases of palliative PD and in 226 (70.8%) of curative PDs ($p = 0.008$). Perineural invasions were more common in the palliative PD group (93.1%) than in the curative PD group (73.7%) ($p = 0.022$). Perineural invasions with abnormal serum carcinoembryonic antigen (CEA) levels (>5 ng/mL) were also more common in the palliative PD group than in the curative PD group

Table 1

Periampullary adenocarcinoma undergoing PD

	Total PD	Palliative PD	Curative PD	p
Patients	348 (100%)	29 (8.3%)	319 (91.7%)	
Operation type				0.563
Open PD (OPD)	171 (49.1%)	16 (55.2%)	155 (48.6%)	
Robotic PD (RPD)	177 (50.9%)	13 (44.8%)	164 (51.4%)	
Gender				1.000
Female	158 (45.4%)	13 (44.8%)	145 (45.5%)	
Age, year old				0.290
Median	66	68	66	
Range	19–95	45 - 89	19 - 95	
Mean ± SD	66±11	68±12	66±11	
Vascular resection (+)	56 (16.1%)	5 (17.2%)	51 (16.0%)	0.795
Chemotherapy (+)	214 (61.5%)	19 (65.5%)	195 (61.1%)	0.695
Primary tumor				0.001
Pancreatic head adenocarcinoma	178 (51.1%)	25 (86.2%)	153 (48.0%)	
Ampullary adenocarcinoma	112 (32.2%)	2 (6.9%)	110 (34.5%)	
Distal CBD adenocarcinoma	35 (10.1%)	1 (3.4%)	34 (10.7%)	
Duodenal adenocarcinoma	23 (6.6%)	1 (3.4%)	22 (6.9%)	
Tumor size				0.008
≤2 cm	95 (27.3%)	2 (6.9%)	93 (29.2%)	
>2 cm	253 (72.7%)	27 (93.1%)	226 (70.8%)	
Tumor cell differentiation				0.286
Well	40 (11.5%)	2 (6.9%)	38 (11.9%)	
Moderate	227 (65.2%)	17 (58.6%)	210 (65.8%)	
Poor	81 (23.3%)	10 (34.5%)	71 (22.3%)	
Lymph node involvement (+)	197 (56.6%)	21 (72.4%)	176 (55.2%)	0.081
Perineural invasion (+)	262 (75.3%)	27 (93.1%)	235 (73.7%)	0.022
Lymphovascular invasion (+)	201 (57.8%)	21 (72.4%)	180 (56.4%)	0.117
Abnormal serum CA 19-9 > 37 U/mL	215 (61.8%)	21 (72.4%)	194 (60.8%)	0.239
Abnormal serum CEA > 5 ng/mL	85 (24.4%)	14 (48.3%)	71 (22.3%)	0.005

CA 19-9 = carbohydrate antigen 19-9; CBD = common bile duct; CEA = carcinoembryonic antigen; PD = pancreaticoduodenectomy.

Table 2

Multivariate analysis for independent predictors of resection status with pancreaticoduodenectomy for periampullary adenocarcinomas

	p	Odds ratio	95% confidence interval for odds ratio
Primary origin of adenocarcinoma	0.012	0.387	0.185–0.810
Abnorma Serum CEA > 5 ng/mL	0.015	2.670	1.209–5.896
Tumor size	0.166	2.923	0.640–13.343
Perineural invasion	0.351	2.11	0.439–10.151

CEA = carcinoembryonic antigen.

(48.3% vs 22.3%; $p = 0.005$). Among the 178 pancreatic head cancers, the R1 resection rate was 3.4%, with 2.4% (2/82) with RPDs and 4.2% (4/96) with OPDs, and the R2 resection rate was 8.4%, with 11.0% (9/82) with RPDs and 6.3% (6/96) with OPDs ($P = 0.447$). The multivariate analysis showed that only the primary origin of adenocarcinomas and abnormal serum CEA levels (>5 ng/mL) were independent predictors of resection status after PDs in periampullary adenocarcinoma (Table 2).

Table 3 lists the surgical outcomes after PDs for periampullary adenocarcinomas. Compared with curative PDs, palliative PDs had longer operation times (median: 8.0 vs 7.0 hours, $p = 0.033$) and more blood loss (median: 500 vs 260 mL, $p = 0.016$). The surgical risks including surgical mortality (0 vs 2.2%), surgical morbidity (41.4% vs 52.4%), POPF (6.9% vs 11.0%), DGE (3.4% vs 8.2%), PPH (0 vs 4.1%), chyle leakage (13.8% vs 16.0%), and wound infection (10.3% vs 5.3%) showed no significant differences between the palliative and curative PD groups. The R0, R1, and R2 resections accounted for 91.7%, 3.4%, and 4.9%, respectively, of the overall periampullary adenocarcinomas and 85.7%, 5.7%, and 8.6%, respectively, of the pancreatic head adenocarcinoma.

Table 3

Surgical outcomes for periampullary adenocarcinoma after PD

	Total PD	Palliative PD	Curative PD	*p*
Patients (n)	348 (100%)	29 (8.3%)	319 (91.7%)	
Operation time (h)				0.033
Median (range)	7.0 (3.9–16.3)	8.0 (6.0–12.8)	7.0 (3.9–16.3)	
Mean ± SD	7.5 ± 2.1	8.3 ± 1.6	7.4 ± 2.1	
Blood loss (c.c.)				0.016
Median (range)	267 (0–2700)	500 (200 –1200)	260 (0–2700)	
Mean ± SD	382 ± 355	534 ± 317	368 ± 356	
Radicality				<0.001
R0	319 (91.7%)	0	319 (100%)	
Margin > 1 mm	306 (87.9%)	0	282 (88.4%)	
Margin ≤ 1 mm	42 (12.1%)	0	37 (11.6%)	
R1	12 (3.4%)	12 (41.4%)	0	
R2	17 (4.9%)	17 (58.6%)	0	
Lymph node harvested				0.482
Median (range)	17 (10–49)	17 (10–31)	17 (10–49)	
Mean ± SD	18 ± 6	18 ± 6	17 ± 6	
Surgical mortality	7 (2.0%)	0	7 (2.2%)	1.000
Surgical morbidity	179 (51.4%)	12 (41.4%)	167 (52.4%)	0.332
Postoperative complications				0.659
Clavien–Dindo 0	170 (48.9%)	17 (58.6%)	153 (48.0%)	
Clavien–Dindo I	128 (36.8%)	9 (31.0%)	119 (37.3%)	
Clavien–Dindo II	13 (3.7%)	0	13 (4.1%)	
Clavien–Dindo III	27 (7.8%)	3 (10.3%)	24 (7.5%)	
Clavien–Dindo IV	3 (0.9%)	0	3 (0.9%)	
Clavien–Dindo V (death)	7 (2.0%)	0	7 (2.2%)	
POPF				0.754
ISGPF grade B and C	37 (10.6%)	2 (6.9%)	35 (11.0%)	
Delayed gastric emptying				0.713
ISGPS grade B and C	27 (7.8%)	1 (3.4%)	26 (8.2%)	
Postpancreatectomy hemorrhage				0.612
ISGPS grade B and C	13 (3.7%)	0	13 (4.1%)	
Chyle leakage	55 (15.8%)	4 (13.8%)	51 (16.0%)	1.000
Wound infection	20 (5.7%)	3 (10.3%)	17 (5.3%)	0.226
Hospital stay (d)				0.697
Median	24 (6–136)	25 (7–64)	24 (6–136)	
Mean ± SD	27 ± 16	28 ± 16	27 ± 16	

ISGPS = International Study Group of Pancreatic Surgery; PD = pancreaticoduodenectomy; POPF = postoperative pancreatic fistula; R0 = curative resection without residual cancer; R1 = microscopic residual cancer; R2 = gross residual cancer.

Compared with palliative OPDs, palliative RPDs had longer operation times (median: 9.0 vs 7.5 hours, $p = 0.001$) (Table 4). There were no significant differences in the surgical risks and other surgical parameters between RPDs and OPDs among the palliative PD group. Conversely, in the curative resection group (Table 5), compared with curative OPDs, curative RPDs were associated with less blood loss (median: 160 vs 400 mL, $p < 0.001$), a greater yield of harvested lymph nodes (median: 17 vs 15, $p = 0.002$), less postoperative complications (46.3% vs 58.1%, $p = 0.046$), less DGE (3.7% vs 12.9%, $p = 0.046$), and shorter hospital stays (median: 23 vs 26 days, $p = 0.031$).

The survival data related to resection status are summarized in Table 6. For pancreatic head adenocarcinoma, there were significant survival differences between only the R0 and R2 resections, while there were no differences between the R0 and R1 and between the R1 and R2 resections (Fig. 1). For the curative R0 resection, the 1-mm margin had no survival impact on the pancreatic head adenocarcinoma.

Table 4

Surgical outcomes for periampullary adenocarcinoma after palliative PD

	Total palliative PD	Robotic palliative PD	Open palliative PD	*p*
Patients (n)	29 (100%)	13 (44.8%)	16 (55.2%)	
Operation time (h)				0.001
Median (range)	8.0 (6.0–12.8)	9.0 (8.0–12.8)	7.5 (6.0–9.5)	
Mean ± SD	8.3 ± 1.6	9.3 ± 1.3	7.5 ± 1.3	
Blood loss (cc)				0.543
Median (range)	500 (200–1200)	400 (200–1200)	500 (200–1100)	
Mean ± SD	534 ± 317	493 ± 321	567 ± 319	
Radicality				0.092
R0	0	0	0	
Margin > 1 mm	0	0	0	
Margin ≤ 1 mm	0	0	0	
R1	12 (41.4%)	3 (23.1%)	9 (56.2%)	
R2	17 (58.6%)	10 (76.9%)	7 (43.8%)	
Lymph node harvested				0.619
Median (range)	17 (10-31)	16 (10–30)	18 (12–31)	
Mean ± SD	18 ± 6	18 ± 6	19 ± 6	
Surgical mortality	0	0	0	N/A
Surgical morbidity	12 (41.4%)	6 (46.2%)	6 (37.5%)	0.716
Postoperative complications				0.715
Clavien–Dindo 0	17 (58.6%)	7 (58.6%)	10 (62.5%)	
Clavien–Dindo I	9 (31.0%)	9 (31.0%)	5 (31.3%)	
Clavien–Dindo II	0	0	0	
Clavien–Dindo III	3 (10.3%)	3 (10.3%)	1 (6.3%)	
Clavien–Dindo IV	0	0	0	
Clavien–Dindo V (death)	0	0	0	
POPF				1.000
ISGPF grade B and C	2 (6.9%)	1 (7.7%)	1 (6.3%)	
Delayed gastric emptying				1.000
ISGPS grade B and C	1 (3.4%)	0	1 (6.3%)	
Postpancreatectomy hemorrhage				
ISGPS grade B and C	0	0	0	N/A
Chyle leakage	4 (13.8%)	2 (15.4%)	2 (12.5%)	1.000
Wound infection	3 (10.3%)	2 (15.4%)	1 (6.3%)	0.573
Hospital stay (d)				0.234
Median	25 (7–64)	24 (7–46)	28 (9–64)	
Mean ± SD	28 ± 16	24 ± 13	32 ± 19	

ISGPS = International Study Group of Pancreatic Surgery; PD = pancreaticoduodenectomy; POPF = postoperative pancreatic fistula; R0 = curative resection without residual cancer; R1 = microscopic residual cancer; R2 = gross residual cancer.

Table 5

Surgical outcomes for periampullary adenocarcinoma after curative PD

	Total curative PD	Robotic curative PD	Open curative PD	p
Patients (n)	319 (100%)	164 (51.4%)	155 (48.6%)	
Operation time (h)				0.808
Median (range)	7.0 (3.9–16.3)	7.5 (3.9–16.3)	6.5 (4.0–15.3)	
Mean ± SD	7.4 ± 2.1	7.9 ± 2.3	7.0 ± 1.7	
Blood loss (cc)				<0.001
Median (range)	260 (0–2700)	160 (0–1500)	400 (75–2700)	
Mean ± SD	368 ± 356	222 ± 220	522 ± 405	
Radicality				N/A
R0	319 (100%)	164 (100%)	155 (100%)	
Margin > 1 mm	282 (88.4%)	142 (86.6%)	140 (90.3%)	
Margin ≤ 1 mm	37 (11.6%)	22 (13.4%)	15 (9.7%)	
R1	0	0	0	
R2	0	0	0	
Lymph node harvested				0.002
Median (range)	17 (10–49)	17 (10–49)	15 (10–40)	
Mean ± SD	17 ± 6	18 ± 6	16 ± 5	
Surgical mortality	7 (2.2%)	4 (2.4%)	3 (1.9%)	1.000
Surgical morbidity	167 (52.4%)	78 (47.6%)	89 (57.4%)	0.093
Postoperative complications				0.046
Clavien–Dindo 0	153 (48.0%)	88 (53.7%)	65 (41.9%)	
Clavien–Dindo I	119 (37.3%)	50 (30.5%)	69 (44.5%)	
Clavien–Dindo II	13 (4.1%)	4 (2.4%)	9 (5.8%)	
Clavien–Dindo III	24 (7.5%)	15 (9.1%)	9 (5.8%)	
Clavien–Dindo IV	3 (0.9%)	2 (1.2%)	1 (0.69%)	
Clavien–Dindo V (death)	7 (2.2%)	5 (3.0%)	2 (1.3%)	
POPF				1.000
ISGPF grade B and C	35 (11.0%)	18 (11.0%)	17 (11.0%)	
Delayed gastric emptying				0.003
ISGPS grade B and C	26 (8.2%)	6 (3.7%)	20 (12.9%)	
Postpancreatectomy hemorrhage				
ISGPS grade B and C	13 (4.1%)	7 (4.3%)	6 (3.9%)	1.000
Chyle leakage	51 (16.0%)	28 (17.1%)	23 (14.8%)	0.648
Wound infection	17 (5.3%)	6 (3.7%)	11 (7.1%)	0.215
Hospital stay (d)				0.031
Median	24 (6–136)	23 (6–82)	26 (8–136)	
Mean ± SD	27 ± 16	25 ± 15	29 ± 17	

ISGPS = International Study Group of Pancreatic Surgery; PD = pancreaticoduodenectomy; POPF = postoperative pancreatic fistula; R0 = curative resection without residual cancer; R1 = microscopic residual cancer; R2 = gross residual cancer.

Table 6

Survival outcomes for periampullary adenocarcinoma after PD

Periampullary adenocarcinoma	1-year survival (%)	5-year survival (%)	Median (month)	Mean + SD (month)	p
Pancreatic head (n = 175)	76.0	21.6	14.2	18.7 + 15.0	0.001
R0 (n = 150)	79.8	22.8	15.8	19.2 + 14.3	R0 vs R1 = 0.306
Margin > 1 mm (n = 119)	77.9	26.2	15.1	18.7 + 15.1	0.129
Margin ≤ 1 mm (n = 31)	87.1	58.4	13.8	16.4 + 10.5	
R1 (n = 10)	66.7	13.3	14.7	23.2 + 25.2	R1 vs R2 = 0.241
R2 (n = 15)	43.2	14.4	7.8	10.9 + 11.6	R2 vs R0 = 0.001
Ampullary (n = 111)	94.3	68.1	29.5	32.9 + 20.5	0.620
R0 (n = 109)	94.2	67.9	30.7	33.2 + 20.5	N/A
R1 (n = 1)	0	N/A	10.2	N/A	N/A
R2 (n = 1)	100	N/A	24.0	N/A	N/A
Distal CBD (n = 33)	93.1	68.3	22.3	31.3 + 23.4	0.286
R0 (n = 32)	92.9	72.3	22.1	31.4 + 23.8	N/A
R1 (n = 0)	N/A	N/A	N/A	N/A	N/A
R2 (n = 1)	100	N/A	26.7	N/A	N/A
Duodenal (n = 22)	76.1	N/A	18.5	21.1 + 14.5	0.537
R0 (n = 21)	74.9	42.1	17.9	20.4 + 14.6	N/A
R1 (n = 1)	100	N/A	34.4	N/A	N/A
R2 (n = 0)	N/A	N/A	N/A	N/A	N/A

CBD = common bile duct; R0 = curative resection without gross and microscopic cancer at the resection margin; R1 = palliative resection without gross, but with microscopic cancer at the resection margin; R2 = palliative resection with gross cancer at the resection margin.

4. DISCUSSION

A curative R0 PD has been regarded as the only hope for the survival of patients with pancreatic adenocarcinoma. Hence, it was the most important factor considered by surgeons in determining the outcome of pancreatic adenocarcinoma;[5] however, a negative-margin resection was not always achieved. The rate of positive margins after PDs for pancreatic cancer was reportedly 15%–85%.[7,13,14,16,24–26] In this study, the R0, R1, and R2 resections accounted for 91.7%, 3.4%, and 4.9%, respectively, of the overall periampullary adenocarcinomas and 88.2%, 3.4%, and 8.4%, respectively, for pancreatic head adenocarcinomas. One of the reasons for the lower rate of R1 resections may have been vascular resections with a radical intent as soon as vascular invasions were suspected. In our study, compared with curative resections, palliative PDs showed a significant association with pancreatic head adenocarcinomas, larger tumors with sizes > 2 cm, more perineural invasions, and higher abnormal serum CEA levels (>5 ng/mL). From the multivariate analysis, only primary tumor origins (pancreatic head adenocarcinoma) and abnormal serum CEA levels (>5 ng/mL) were independent predictors of resection status after PDs for periampullary adenocarcinoma. The higher incidence of palliative resections for pancreatic head adenocarcinomas may be attributed to both biologic behavior and the anatomic approximation of the superior mesenteric vessels. This may occur in the following instances: (1) a competent surgeon may perform a macroscopically radical operation with a curative intention; however, the final microscopic examination may have reported it to be an unexpected R1 resection; (2) an aggressive surgeon with sufficient ability may perform the operation to the "point of no return," dividing the pancreatic neck and, ultimately, completed the operation by performing a palliative PD; (3) a palliative PD may have been required for an active complication, such as tumor-related bleeding;[7] (4) an R2 palliative PD may have been planned for patients with isolated liver metastases and resectable primary periampullary adenocarcinomas if there were multiple choices of advanced treatment modalities for the liver metastasis in addition to systemic chemotherapy, such as radiofrequency ablation, alcohol injection, and Yttrium-90 (Y90) radioembolization therapy.[27–29]

Most (58%–88%) palliative PDs for pancreatic head adenocarcinoma were, typically, because of positive margins along the superior mesenteric vein/artery and portal vein.[9,14,30] Theoretically, vascular resections can increase R0 resection rates. However, our experience suggested that vascular resections did not necessarily lead to higher R0 resection rates. In this study, the vascular resection rate was 17.2% for palliative PDs and 16.0% for curative PDs. In practice, not all surgeons advocate performing a vascular resection during a PD, as it is still a matter of controversy in terms of surgical risks and survival outcomes.[7] Our study showed that not only anatomical factors including primary tumor origin and tumor sizes but also biologic factors including perineural invasions and abnormal serum CEA levels can be risk factors associated with positive resection margin; only one anatomical factor, primary tumor origin, and one biologic factor, abnormal serum CEA levels, remained

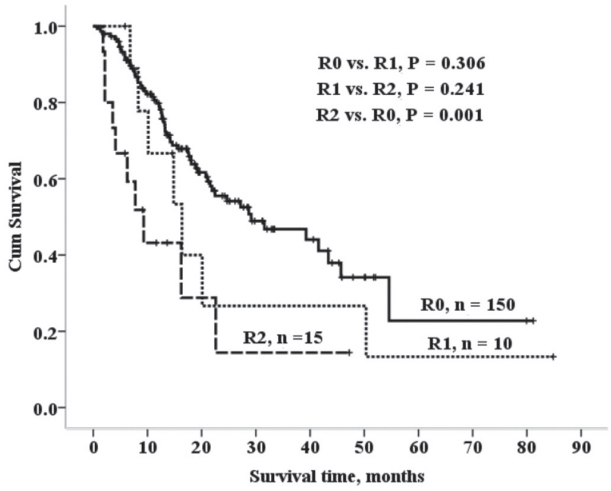

Fig. 1 Survival curves for pancreatic head adenocarcinoma after R0, R1, and R2 resections. R0: curative resection without gross and microscopic cancer at the resection margin; R1 = palliative resection without gross, but with microscopic cancer at the resection margin; R2 = palliative resection with gross cancer at the resection margin.

as independent predictors of resection status. These findings implied that the anatomic location and biologic behavior of the tumor as well as the surgical techniques used may play a role in achieving a negative-margin resection.

The surgical risk is one of the major concerns in performing palliative PDs. In our study, the surgical risks including surgical morbidity, POPF, DGE, PPH, chyle leakage, and wound infection were similar between the palliative and curative PD groups. There was no surgical mortality following palliative PDs, while there was surgical mortality in 2.2% of cases following curative PD. Therefore, the surgical mortality rates of either palliative or curative PDs are no longer unacceptable. Nevertheless, considering that the overall surgical morbidity was still high (41.4% in palliative PD and 52.4% in curative PD), PDs should be carefully considered for each individual patient. Furthermore, the surgeon's ability and patient's characteristics should also be included in the assessment of the surgical risk of PDs.[7] In our palliative PD groups, the surgical risks were similar between the RPD and OPD. Moreover, when compared with the OPD in our curative PD group, the RPD was associated with less blood loss, a higher yield of harvested lymph nodes, a lower DGE, and shorter hospital stays. These findings indicate that RPD can be a choice of technique, not only for curative but also for palliative resections.

A major operation like PD cannot be justified without survival benefits. The impact of palliative PDs, either R1 or R2 resections, on the survival outcome is still unclear.[7,8,14,25,30] Lillemoe et al. reported that palliative PDs and bypass operations shared similar perioperative morbidity and mortality rates but better long-term survival in patients who received palliative PDs than in those who only had surgical bypasses. Their findings supported the role of palliative PDs in pancreatic carcinomas.[8] Likewise, Butturini et al. found that there was no difference in the overall survival between R0 and R1 after chemotherapy.[6,30,31] Further, Raut et al.[14] suggested that there was no significant difference in patient survival or recurrence based on resection status. Similarly, Kato et al.[13] reported that it was the R2, not R1, resection that affected the survival outcome in the multivariate analysis, independently. In this study, the survival outcome after the R1 resection was not inferior to R0 for pancreatic head adenocarcinoma, while the R2 resection was associated with a worse survival outcome for pancreatic head adenocarcinoma.

In conclusion, an R1 resection can be performed to improve the survival outcome. Conversely, based on our findings and previous studies, performing an R2 resection was not recommended.[12,13,16,17] The discrepancies between pancreatic and periampullary adenocarcinomas may imply that not only the resection margin but also the tumor biology can determine the survival outcome of pancreatic head adenocarcinoma, which might have been, in most patients, already a systemic disease at the time of performing the operation. Palliative treatment can be the ultimate choice for the vast majority of patients regardless of the resection margin, considering that the aggressiveness of pancreatic head adenocarcinoma would most likely result in poor survival outcomes for most patients, despite them undergoing potentially curative R0 PDs.[7] Thus, while the prognostic effect of R0 vs R1 seemed to decline in larger trials, adjuvant chemotherapy became the standard treatment for patients with either R0 or R1 resections for pancreatic cancer.[6,8,14,30]

There was intercontinental difference in the definitions of R0, which is a 0-mm tumor distance from the resection margin in the United States; however, Europe, the United Kingdom, and Australia accepted a definition based on a 1-mm clearance and report the margin status as R1 if microscopic cancer cells are present within 1 mm from resection margin.[6,26,32–35] Our findings showed that the 1-mm margin had no survival impact on pancreatic head adenocarcinoma.

In conclusion, surgical risks were similar between the palliative and curative PD groups. The survival after an R1 resection was not necessarily inferior to that after an R0 resection for pancreatic head adenocarcinoma, while an R2 resection was associated with worse outcomes for pancreatic head adenocarcinoma. Our findings supported the role of palliative R1 PDs for pancreatic head adenocarcinoma in terms of surgical risks and survival outcomes. However, R2 PDs should be avoided.

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