Published in final edited form as:

Ann Surg Oncol. 2010 December ; 17(12): 3112–3119. doi:10.1245/s10434-010-1200-3.

Adjuvant Chemoradiation Therapy for Adenocarcinoma of the Distal Pancreas

Kristin J. Redmond, MD, MPH¹, Christopher L. Wolfgang, MD, PhD², Elizabeth A. Sugar, PhD^{3,4}, Julia Ahn, BA¹, Hari Nathan, MD², Daniel Laheru, MD², Barish H. Edil, MD², Michael A. Choti, MD², Timothy M. Pawlik, MD², Ralph H. Hruban, MD⁵, John L. Cameron, MD², and Joseph M. Herman, MD, MSc¹

¹Department of Radiation Oncology and Molecular Radiation Sciences, The Sol Goldman Pancreatic Cancer Research Center, The Johns Hopkins University School of Medicine, Baltimore, MD

²Department of Surgery, The Sol Goldman Pancreatic Cancer Research Center, The Johns Hopkins University School of Medicine, Baltimore, MD

³Department of Epidemiology, The Bloomberg School of Public Health, The Johns Hopkins University, Baltimore, MD

⁴Department of Biostatistics, The Bloomberg School of Public Health, The Johns Hopkins University, Baltimore, MD

⁵Department of Pathology, The Sol Goldman Pancreatic Cancer Research Center, The Johns Hopkins University School of Medicine, Baltimore, MD

Abstract

Background—This study was designed to examine the effect of adjuvant 5-FU-based chemoradiation therapy (CRT) after distal pancreatectomy for adenocarcinoma of the distal pancreas.

Methods—All patients underwent curative resection for adenocarcinoma of the distal pancreas between December 1985 and June 2006. Patients who received adjuvant CRT were compared with those who underwent surgery alone. A Kaplan–Meier estimate of the survival curve was used to determine estimates of the median survival and proportion alive at 1 and 2 years; log-rank tests were used to make comparisons between groups.

Results—A total of 123 patients underwent distal pancreatectomy; 29 patients were excluded for distant metastases at the time of surgery ($n = 12$, 10%) or before adjuvant therapy ($n = 11$, 9%), death within 2 months of surgery ($n = 2$, 2%), or if CRT treatment status was unknown ($n = 4$, 3%). Of the remaining 94 patients, 72% received adjuvant 5-FU-based CRT and 28% underwent surgery alone. Overall median survival was 16.2 (95% confidence interval (CI), 13.1–18.9) months. The groups were similar with respect to tumor size, nodal status, and margin status. There was no significant difference in overall survival between patients treated with adjuvant CRT versus surgery alone ($p = 0.23$). An exploratory subgroup analysis suggested a potential survival benefit of adjuvant CRT in patients with lymph node metastases (16.7 vs. 12.1 months, $p < 0.01$).

Conclusions—Adjuvant CRT did not increase survival compared with surgery alone; however, patients with node-positive disease appear to benefit from adjuvant CRT.

The overall prognosis of adenocarcinoma of the body and the tail of the pancreas is poor.^{1,2} Pancreatic head lesions typically produce biliary obstruction and subsequent jaundice. Conversely, tumors of the body and tail of the pancreas rarely cause obstructive symptoms and often are diagnosed at advanced stages. Because the pancreatic body lies in close proximity to the celiac axis and mesenteric vessels, it is common for carcinomas in this location to be large and unresectable at presentation.³ In patients with resectable carcinomas, surgery provides a chance of cure, but survival after surgery alone is dismal with high rates of recurrence and distant metastases.¹⁻³

Limited studies to date have analyzed outcomes in patients with adenocarcinoma of the distal pancreas.¹⁻³ Furthermore, the impact of specific risk factors on survival has been inconsistent. Given the paucity of data regarding the efficacy of adjuvant therapy after a distal pancreatectomy, current recommendations regarding adjuvant therapy are extrapolated from studies composed predominantly of adenocarcinoma of the head of the pancreas, many of which show conflicting results.⁴⁻⁷

This study was designed to examine risk factors for disease progression and to evaluate whether adjuvant 5-FU-based chemoradiation therapy (CRT) improves overall survival for adenocarcinoma of the body and tail of the pancreas.

METHODS

Between December 18, 1985 and June 13, 2006, 123 patients underwent distal pancreatectomy for adenocarcinoma of the body or tail of the pancreas at the Johns Hopkins Hospital (JHH). All patients underwent resection of a carcinoma that was located in the distal neck, body, or tail of the pancreas. In all cases a lymphadenectomy was performed, and in 98% of the cases the spleen was resected en bloc with the pancreas. The preoperative determination of resectability was most commonly performed by using CT angiography and less commonly by MRI.⁸ These studies were supplemented with endoscopic ultrasound as necessary. In some cases, laparoscopy was used to evaluate for the presence of suspected carcinomatosis before resection. Patients who were preoperatively deemed resectable were considered surgically unresectable if distant metastasis or >180 degrees of circumferential involvement of the superior mesenteric artery or celiac axis was identified at the time of surgery. Involvement of the portomesenteric vein in the absence of arterial involvement was not a contraindication for resection. Tumors infiltrating adjacent organs, such as the stomach, liver, colon, and kidney, were considered resectable as long as technically feasible.

Approval was granted by the Johns Hopkins Hospital Institutional Review Board before data collection. Patients were excluded if they were found to have M1 disease at the time of surgery ($n = 12$) or during the preadjuvant therapy workup ($n = 11$), if they died within 60 days of surgery ($n = 2$), or if it was unknown whether they had received adjuvant therapy ($n = 3$). The final study cohort included 94 patients. Among them, 26 (28%) received no adjuvant therapy, 29 (31%) underwent 5-FU-based CRT at Johns Hopkins, and 39 (41%) underwent CRT at an outside facility. Because patient characteristics did not differ significantly for those who received adjuvant therapy at JHH or at other institutions, the groups were combined for further analysis.

Preoperative data were collected prospectively at the time of surgery. Severe comorbid conditions evaluated included second malignancies, coronary artery disease, chronic obstructive pulmonary disease, and cerebrovascular accidents. Length of hospital stay was evaluated.

Pathologic data evaluated included tumor size, lymph node status, resection margins, stage, grade, perineural, and perivascular invasion. A lymph node was considered positive for

metastasis if it contained carcinoma, including direct extension in continuity with the primary tumor. Resection margins were considered positive if invasive carcinoma was present at any single margin.

Postoperatively, most patients were evaluated by radiation and medical oncology and were offered adjuvant therapy according to the JHH standard at the time of their evaluation, which generally consisted of concurrent 5-FU with radiation followed by maintenance 5-FU for an additional 2–6 months. For patients treated at another hospital, the same treatment recommendations were given and typically communicated via dictated consultation to the treating physician. Patients who elected to receive no therapy did so after being fully informed about the potential risks and benefits of choosing not to receive further therapy.

For those patients who received radiation therapy at JHH, the clinical treatment volume (CTV) was defined as the preoperative tumor bed, pancreaticoduodenal lymph nodes, splenic hilar lymph nodes, suprapancreatic lymph nodes, and the proximal celiac and superior mesenteric arteries. This was expanded by 1.5 cm for the final planning treatment volume (PTV1). At Johns Hopkins, the preliminary volume was typically treated to 45–50.4 Gy, and in select cases there was a second cone-down (PTV2) to the tumor bed plus a 1–1.5-cm margin to 50–54 Gy. The median total dose for our cohort was 48.6 (range, 37–60) Gy. Forty-one percent of patients had treatment breaks during radiation therapy. Seventy-five percent of these treatment breaks were planned as patients were treated according to the Gastrointestinal Tumor Study Group.⁷ In this study patients were given a 2-week break after the first 2 weeks of treatment. The details of therapy could not be fully assessed for patients treated elsewhere.

Patient follow-up was obtained from hardcopy charts and electronic medical records. Survival was determined and cross-checked by review of clinical follow-up information, cancer center abstracting services, and the Social Security Death Index. Site of first failure was recorded when available from follow-up notes, imaging studies, pathology reports, or correspondences.

STATISTICAL METHODS

Summary statistics for continuous and categorical variables were calculated. Comparisons were performed using Fisher's exact test for categorical variables and the Wilcoxon rank-sum test for continuous variables. The number of individuals with missing data is recorded for each variable and all summary statistics and tests of comparison are based on only the individuals with known covariates.

The primary outcome was overall survival, which was defined as the time from distal pancreatectomy until death. Patients were censored at the date of last known follow-up or death. A Kaplan–Meier estimate of the survival curve was computed and used to calculate median overall survival, as well as 1- and 2-year survival proportions with 95% confidence intervals. Comparisons between groups were made using the log-rank test. Cox proportional hazards modeling was used to model the effect of treatment while adjusting for other covariates. Similar analyses were performed for disease-free survival, defined as the time from surgery until disease recurrence.

RESULTS

All patients underwent distal pancreatectomy for adenocarcinoma of the body or the tail of the pancreas. Table 1 shows baseline patient, surgical, and pathologic tumor characteristics for the entire cohort and stratified by treatment group. The median age at the time of surgery was 68 (range, 26–92) years. Forty-six percent of patients were men, and 87% were white.

Severe comorbid disease was present in 28% of patients at the time of presentation. Ninety-eight percent underwent splenectomy and 16% underwent bowel resection. The median length of hospital stay was 7 (range, 5–110) days. Those who did and did not receive adjuvant therapy were similar with respect to known poor prognostic factors. The only statistically significant difference between the adjuvant CRT and no CRT group was that more patients in the adjuvant CRT group were white ($p = 0.02$). Tumor size was >3 cm in 76% of patients. Positive margins were identified in 29% of patients and 55% had lymph node metastases. Because the American Joint Committee on Cancer (AJCC) staging manual was updated in 2002, staging before this date was updated for consistency.

Overall median survival for the entire cohort was 16.2 (95% CI, 13.1–18.9) months. One-year overall survival was 62% and 2-year overall survival was 31%. The influence of patient- and treatment-specific factors on survival is presented in Table 2. Age and race did not significantly affect survival in our analysis. Female gender was associated with a significantly better overall survival ($p = 0.05$) as was severe comorbid disease ($p = 0.04$).

There was no statistically significant difference in median, 1-, or 2-year overall survival for patients treated with adjuvant CRT compared with surgery alone (16.7 vs. 12.1 months; 66% vs. 50%, 29% vs. 32%, $p = 0.23$), respectively (Fig. 1). After adjusting for age, gender, race, node, and margin status, there remained no significant difference in overall survival between patients who received adjuvant CRT and those treated with surgery alone (hazards ratio (HR) = 0.61; 95% CI, 0.34–1.08; $p = 0.09$).

To determine whether our results varied based on location of adjuvant therapy (JHH vs. elsewhere), we performed two subgroup analyses. First, we compared the characteristics and survival for patients who received adjuvant therapy at JHH and elsewhere. Some differences in patient characteristics were observed between those treated with adjuvant therapy at JHH versus elsewhere (node positive: 46% vs. 54%, $p = 0.61$; margin positive: 12% vs. 39%, $p = 0.02$; and age >65 years: 41% vs. 64%, $p = 0.09$). On univariate analysis, there was a significant survival benefit for patients treated at JHH versus elsewhere (21.5 vs. 14.5 months; HR, 0.46; 95% CI, 0.26–0.82; $p < 0.01$); however, this benefit was not significant after adjusting for age, gender, race, and nodal and margin status (HR, 0.52; 95% CI, 0.26–1.02; $p = 0.06$). Second, we attempted to replicate our primary results using only individuals who received adjuvant CRT at JHH (excluded elsewhere CRT). In this case, there was a significant increase in survival with adjuvant CRT at JHH vs. observation (21.5 vs. 12.1 months; HR, 0.51; 95% CI, 0.27–0.97; $p = 0.04$); however, this association was not significant after adjusting for age, gender, race, and nodal and margin status (HR, 0.59; 95% CI, 0.28–1.23; $p = 0.16$). The effects on survival observed for age, gender, race, and margin status and the interaction between nodal status and treatment were similar to those obtained using the entire cohort with a slight loss of power as would be expected due to the reduction in sample size. Therefore, we thought it was reasonable to combine patients who received adjuvant therapy at JHH and elsewhere in the final analysis.

Although the study was not designed to detect interactions between therapy type and risk factors, exploratory analyses were performed. Table 3 displays the median overall survival for patients receiving adjuvant CRT versus surgery alone by risk factors. There is a significant interaction between node status and treatment ($p < 0.01$) indicating that patients respond differently to therapy depending upon nodal status. Figure 2 shows the overall survival for patients in the CRT versus surgery alone arms for node-positive individuals. Both alone and after adjusting for age, gender and margin status, there was a significant improvement in overall survival for node-positive patients treated with adjuvant CRT versus surgery alone (HR, 0.28; 95% CI, 0.14–0.58; $p < 0.01$; and HR, 0.23; 95% CI, 0.1–0.52; $p < 0.01$, respectively). For node-negative individuals, the sample size was extremely small ($N =$

8 for the surgery alone and $N = 31$ adjuvant chemoradiation therapy). In fact, only three deaths were observed from eight subjects in the surgery alone group. Nevertheless, univariate analysis indicated that there might be a survival benefit for the surgery alone arm (HR, 3.0; 95% CI, 0.9–10; $p = 0.06$). The results above were nearly identical when the analysis was restricted to JHH patients (results not shown).

The data were missing for a number of individuals for several key variables (e.g., 16 for tumor diameter, 7 for node and margin status). Multiple imputation with ten replicates was used to determine the impact of the missing data on the estimated effects. These analyses produced estimates that were nearly identical to those found using the observed data (results not shown).

Data on patterns of failure were available for 35 patients (10 surgery and 24 adjuvant therapy). There was no significant difference in time to relapse between the surgery alone and CRT groups, respectively (median, 4.8 vs. 9.8 months; $p = 0.08$). Of all patients with recorded recurrences, 12 were local, 21 were distant, and 1 patient had both a local and distant recurrence. Of patients with distant recurrences the majority were liver,¹⁰ one was at an unknown site, and ten were defined as other, including peritoneal involvement, omental seeding, or lung metastasis. Stratifying by CRT, 6 of 10 (60%) failures occurred in the surgery only group versus 6 of 24 (25%) for the adjuvant CRT group.

DISCUSSION

We present the most comprehensive study of adjuvant therapy after distal pancreatectomy for adenocarcinoma of the body and the tail of the pancreas to date. We do not show a significant survival benefit with adjuvant 5-FU-based CRT. We did, however, show a potential benefit of adjuvant CRT in patients with lymph node metastasis.

There is a paucity of data regarding adjuvant therapy after distal pancreatectomy for adenocarcinoma of the body or tail of the pancreas. The recent Radiation Therapy Oncology Group randomized trial (97-04) excluded patients with tumors of the distal pancreas from the analysis.⁹ Retrospective reviews designed to explore adjuvant or neoadjuvant therapy for distal pancreatic tumors have been small, ranging in size from 7 to 30 patients.^{2,3} As such, we believe our study represents an important contribution to the literature.

Limited studies have analyzed outcomes in patients with adenocarcinoma of the distal pancreas.^{1–3, 10–15} The largest series to date is a surgical series of 93 patients from Christein et al., which was designed to evaluate the role of en bloc resection in the surgical management of three subtypes of pancreatic adenocarcinoma (mucinous cystadenocarcinoma or adenocarcinoma with intraductal papillary mucinous neoplasms).¹ On univariate analysis the authors found age, tumor size, and stage to be significant predictors of survival. These differences were not significant after adjusting for multiple variables. Presence of lymph node (LN) metastases or positive margin did not significantly affect survival in their study. This is consistent with our results; however, there was a trend toward inferior survival seen in patients with margin-positive resections ($p = 0.07$).

On univariate analysis there was a significant difference in survival for those patients who received adjuvant therapy at JHH vs. elsewhere. However, this difference was no longer significant after controlling for nodal and margin status on multivariate analysis. It should be noted that despite the difficulties in following patients at other treatment facilities the follow-up was censored (patients alive at last follow-up) for only 4 of 39 (10%) patients. This total compares favorably to the rates observed for those who did not receive radiation therapy (7/27, 27%) and those who did receive therapy at JHH (9/29, 31%). Despite the observed survival differences based on treatment location, the effect of the other prediction

variables (nodal status, margin status, etc.) was consistent when considering the cohort as a whole (JHH and elsewhere) or analyzing the JHH alone cohort.

Christein et al. report in their discussion that 74% of their patients received adjuvant therapy.¹ The median OS with adjuvant therapy in their study was 16.2 vs. 11.8 months without adjuvant therapy ($p = 0.3$). These results are consistent with our study (16.7 vs. 12.1). It is difficult however to draw specific conclusions regarding the role of adjuvant therapy from their study because there were no details regarding adjuvant therapy, and the authors did not statistically account for the different tumor types, risk factors, or selection bias.

Our data highlight the poor survival of patients with adenocarcinoma of the distal pancreas irrespective of adjuvant therapy. We report an overall median survival of 16.2 months, which is comparable to that found in previous studies. For example, a surgical series of 44 patients¹⁰ demonstrated a median overall survival of 10 months, 2-year overall survival of 15%, and 5-year overall survival of 8% after distal pancreatectomy for adenocarcinoma of the body or tail of the pancreas.

It is concerning that 23 of 123 patients (19%) who underwent a distal pancreatectomy in our study were excluded from the analysis because they had metastatic disease at the time of surgery or before initiation of adjuvant therapy. This suggests limitations in current preoperative staging paradigms and raises the importance of better selection of patients for curative resection.

There are several limitations of the current study. First, the analysis of CRT was retrospective in nature. As a result, some patients were lost to follow-up and treatment was not randomized. However, every effort was made to identify patients who died by reviewing the electronic medical record, the cancer registry, and the Social Security Death Index. In addition, because of variations in reporting within the institution during the study period, some measurements (e.g., tumor stage) were not observed for all individuals. Multiple imputation techniques showed similar results to the complete data techniques, which indicate that, assuming the data are missing at random (MAR), the conclusions are robust. Second, although all of the patients were treated with concurrent 5-FU-based chemotherapy, the regimens varied between patients. Some patients received additional agents on a clinical trial and some received maintenance gemcitabine as opposed to 5-FU. Third, radiation techniques and doses likewise varied between patients. Finally, although this is the largest single center series reported to date, the sample size is limited, which makes it difficult to detect small effects.

In summary, our data do not show a significant improvement in overall survival with adjuvant 5-FU-based CRT after distal pancreatectomy compared with distal pancreatectomy alone. In an exploratory analysis, patients with node metastases seemed to potentially benefit from adjuvant CRT, which merits further study. A large percentage of patients were found to have distant metastasis at the time of surgery or before initiation of adjuvant therapy, suggesting a need for more extensive evaluation before surgery or perhaps consideration of neoadjuvant therapy to better select patients for subsequent resection.¹⁶

References

1. Christein JD, Kendrick ML, Iqbal CW, Nagorney DM, Farnell MD. Distal pancreatectomy for resectable adenocarcinoma of the body and tail of the pancreas. *J Gastrointest Surg*. 2005; 9:922–7. [PubMed: 16137585]
2. Ozaki H, Kinoshita T, Kosuge T, et al. An aggressive therapeutic approach to carcinoma of the body and tail of the pancreas. *Cancer*. 1996; 77:2240–5. [PubMed: 8635090]

3. Arnoletti JP, Hoffman JP, Ross EA, et al. Preoperative chemo-radiation in the management of adenocarcinoma of the body of the pancreas. *Am Surg.* 2002; 68:330–6. [PubMed: 11952242]
4. Klinkenbijl JH, Jeekel J, Sahmoud T, et al. Adjuvant radiotherapy and 5-fluorouracil after curative resection of cancer of the pancreas and perampullary region: phase III trial of the EORTC gastrointestinal tract cancer cooperative group. *Ann Surg.* 1999; 230:776–82. [PubMed: 10615932]
5. Neoptolemos JP, Dunn JA, Stocken DD, et al. Adjuvant chemoradiotherapy and chemotherapy in resectable pancreatic cancer: a randomized controlled trial. *Lancet.* 2001; 358:1576–85. [PubMed: 11716884]
6. Herman JM, Swartz MJ, Hsu CC, et al. Analysis of fluorouracil-based adjuvant chemotherapy and radiation after pancreaticoduodenectomy for ductal adenocarcinoma of the pancreas: results of a large prospectively collected database at the Johns Hopkins Hospital. *J Clin Oncol.* 2008; 26:3503–10. [PubMed: 18640931]
7. Kalser MH, Ellenberg SS. Pancreatic cancer: adjuvant combined radiation and chemotherapy following curative resection. *Arch Surg.* 1985; 120:899–903. [PubMed: 4015380]
8. Fishman EK, Horton KM. Imaging pancreatic cancer: the role of multidetector CT with 3-dimensional CT angiography. *Pancreatology.* 2001; 1:610–24. [PubMed: 12120244]
9. Regine WF, Winter KA, Abrams RA, et al. Fluorouracil vs. gemcitabine chemotherapy before and after fluorouracil-based chemoradiation following resection for pancreatic adenocarcinoma: a randomized controlled trial. *JAMA.* 2008; 299:1019–26. [PubMed: 18319412]
10. Dalton RR, Sarr MG, van Heerden JA, Colby TV. Carcinoma of the body and tail of the pancreas: is curative resection justified? *Surgery.* 1992; 111:489–94. [PubMed: 1317976]
11. Diener MK, Knaebel HP, Witte ST, et al. DISPACT trial: a randomized controlled trial to compare two different surgical techniques of DIStal PAnCreaTectomy—study rationale and design. *Clin Trials.* 2008; 5:534–45. [PubMed: 18827046]
12. Pugliese R, Maggioni D, Sansonna F, et al. Laparoscopic distal pancreatectomy: a retrospective review of 14 patients. *Surg Laparosc Endosc Percutan Tech.* 2008; 18:254–9. [PubMed: 18574411]
13. Johnson CD, Schwall G, Flechtenmacher J, Trede M. Resection for adenocarcinoma of the body and tail of the pancreas. *Br J Surg.* 1993; 80:1177–9. [PubMed: 8402126]
14. Nordback IH, Hruban RH, Boitnott JK, et al. Carcinoma of the body and tail of the pancreas. *Am J Surg.* 1992; 164:26–31. [PubMed: 1378243]
15. Brennan MF, Moccia RD, Klimstra D. Management of adenocarcinoma of the body and tail of the pancreas. *Ann Surg.* 1996; 223:506–12. [PubMed: 8651741]
16. Rose DM, Delbeke D, Beauchamp RD, Chapman WC, Sandler MP, Sharp KW, Richards WO, Wright JK, Frexes ME, Pinson CW, Leach SD. 18Fluorodeoxyglucose-positron emission tomography in the management of patients with suspected pancreatic cancer. *Ann Surg.* 1999; 229(5):729–37. discussion 737–8. [PubMed: 10235532]

FIG. 1.

Kaplan–Meier curves comparing overall survival in patients who received adjuvant radiation therapy versus distal pancreatectomy alone. A total of five patients in the adjuvant chemoradiation therapy group were censored beyond 85 months

FIG. 2. Kaplan–Meier curves comparing treatment groups in node-positive patients. A total of three patients with node-positive disease in the adjuvant chemoradiation therapy group were censored at time points beyond 85 months

TABLE 1

Baseline patient, surgical, and pathologic tumor characteristics for the entire cohort stratified by treatment group

Characteristics	Overall	Chemoradiation	Distal pancreatectomy alone	p value
Demographic				
Age at surgery (yr)				
Mean SD	66.2 (11.8)	65.4 (11.5)	68.3 (12.5)	0.24
Median range	67.2 (26–91.8)	66.3 (35.9–83.5)	70.8 (26–91.9)	
Male	43 (46%)	34 (50%)	9 (35%)	0.25
Race				
White	82 (87%)	63 (93%)	19 (73%)	0.02
Other	12 (13%)	5 (7%)	7 (27%)	
Surgical				
Severe comorbid disease				
Yes	26 (28%)	17 (25%)	9 (35%)	0.44
No	68 (72%)	51 (75%)	17 (65%)	
Hospital stay (days)				
Mean (SD)	10.4 (13.9)	10.2 (13.9)	11.1 (14.1)	0.96
Median (range)	7 (5–110)	7 (5–110)	7 (5–77)	
Unknown	2 (2%)	2 (3%)	0 (0%)	
Tumor pathology				
Tumor diameter (cm)				
Mean (SD)	4.3 (1.9)	4.5 (1.9)	3.8 (1.8)	0.19
Median (range)	4 (0.3–9.5)	4.5 (1–9.5)	3.5 (0.3–8)	
Unknown	16 (17%)	13 (19%)	3 (12%)	
Node status				
Positive	48 (55%)	32 (51%)	16 (67%)	0.23
Negative	39 (45%)	31 (49%)	8 (33%)	
Unknown	7 (7%)	5 (7%)	2 (8%)	
TNM stage				
I/II	79 (93%)	56 (92%)	23 (96%)	0.67
III	6 (7%)	5 (8%)	1 (4%)	
Unknown	9 (10%)	7 (10%)	2 (8%)	
Margin status				
Positive	25 (29%)	18 (29%)	7 (29%)	>0.99
Negative	62 (71%)	45 (71%)	17 (71%)	
Unknown	7 (7%)	5 (7%)	2 (8%)	
Histologic grading				
1–2	39 (51%)	28 (52%)	9 (41%)	0.45
3–4	37 (49%)	26 (48%)	13 (59%)	
Unknown	18 (19%)	14 (21%)	4 (15%)	
Perineural invasion (PNI)				

Characteristics	Overall	Chemoradiation	Distal pancreatectomy alone	<i>p</i> value
Yes	49 (56%)	36 (56%)	14 (58%)	>0.99
No	38 (43%)	28 (44%)	10 (42%)	
Unknown	7 (7%)	5 (7%)	2 (8%)	
Perivascular invasion (PVI)				
Yes	20 (23%)	14 (22%)	6 (25%)	0.78
No	67 (77%)	49 (78%)	18 (75%)	
Unknown	7 (7%)	5 (7%)	2 (8%)	

TABLE 2

Univariate analyses of the associations between overall survival and patient characteristics

Characteristic	N	%	Survival (%)		Survival (mo)		Univariate analysis		p value
			1-year	2-year	Median	95% CI	HR	95% CI	
Overall	94	100	62	31	16.2	(13.1–18.9)			
Age >65 yr									
No	39	42	76	38	17.1	(14.3–32.8)	1.00		0.08
Yes	55	58	52	26	12.9	(10.8–21.7)	1.51	(0.94–2.42)	
Sex									
Female	51	54	67	43	18.9	(13.7–34.5)	1.00		0.05
Male	43	46	56	17	14.3	(11–17.8)	1.59	(1–2.52)	
Race									
Other	12	87	73	55	24	(18.9–Inf)	1.00		0.19
White	82	13	61	28	14.5	(12.6–17.8)	1.62	(0.77–3.4)	
Severe comorbid disease									
No	68	72	56	25	13.7	(11.2–17.1)	1.00		0.04
Yes	26	28	79	46	23.4	(17.1–Inf)	0.58	(0.34–1)	
Tumor diameter (cm)									
<3	19	24	75	38	17.2	(13.7–Inf)	1.00		0.44
>3	59	76	60	29	14.5	(11.6–21.5)	1.28	(0.67–2.42)	
Unknown	16	17			14.8	(7.2–34.5)			
Nodal status									
Negative	39	45	66	37	17.1	(14.7–32.8)	1		0.15
Positive	48	55	60	24	13.7	(11–18.8)	1.42	(0.87–2.3)	
Unknown	7	7			21.7	(7.2 to Inf)			
TNM stage									
I/II	79	93	63	33	16.2	(12.9–21.9)	1		0.38
III	6	7	67	0	17.3	(11 to Inf)	1.46	(0.62–3.44)	
Unknown	9	10			21.7	(7.2 to Inf)			
Histologic grade									
1,2	39	51	72	30	16.5	(14–22.7)	1		0.82
3	37	49	57	40	13.4	(10.8–32.8)	0.94	(0.56–1.58)	

Characteristic	N	%	Survival (%)		Survival (mo)		Univariate analysis		p value
			1-year	2-year	Median	95% CI	HR	95% CI	
Unknown	18	19			13.6	(9–23.4)			
Margin status									
Negative	62	71	68	34	16.5	(13.4–23.4)	1		0.07
Positive	25	29	50	21	13.7	(8.4–18.8)	1.6	(0.96–2.64)	
Unknown	7	7			21.7	(7.2–Inf)			
Perineural invasion									
No	38	44	60	34	15.7	(10.8–24.8)	1.00		0.72
Yes	49	56	64	27	16.2	(12.9–18.9)	1.09	(0.67–1.78)	
Unknown	7	7			21.7	(7.2–Inf)			
Perivascular invasion									
No	67	77	60	30	14.7	(12–18.9)	1		0.5
Yes	20	23	72	28	17.5	(14 to Inf)	0.82	(0.45–1.48)	
Unknown	7	7			21.7	(7.2 to Inf)			

TABLE 3
Comparison of the overall survival between treatment groups stratified by patient characteristics

Characteristic	Patients		Overall survival					
	Distal pancreatectomy alone		Chemoradiation		Distal pancreatectomy alone		Chemoradiation	
	N	%	N	%	Median	95% CI	Median	95% CI
All patients	26	28	68	72	12.1	(10.7–26.1)	16.7	(14.0–21.9)
Age > 65 yr								
No	8	31	31	46	14.0	(11–Inf)	17.1	(15.7–44.7)
Yes	18	69	37	54	10.7	(6.4–Inf)	14.7	(10.8–21.9)
Sex								
Female	17	65	34	50	13.4	(10.7–Inf)	20.2	(14.7–44.7)
Male	9	35	34	40	10.9	(6.6–Inf)	15.7	(11.6–21.7)
Race								
Other	7	27	5	7	18.4	(6.6–Inf)	24.0	(23.4–Inf)
White	19	73	63	93	12.1	(6.4–Inf)	16.2	(12.9–21.5)
Comorbid disease								
No	17	65	51	75	10.8	(6.6–Inf)	15.7	(12.0–21.5)
Yes	9	35	17	25	27.8	(6.1–Inf)	21.9	(17.1–Inf)
Tumor diameter (cm)								
<3	6	26	13	24	NA	(3.7–Inf)	16.5	(14.7–Inf)
>3	17	74	42	76	10.8	(6.6–27.8)	16.7	(13.4–32.8)
Nodal status								
Negative	8	33	31	49	NA	(27.8–Inf)	16.3	(11.7–23.4)
Positive	16	67	32	51	10.7	(6.4–14.3)	17.1	(13.4–34.5)
Margin status								
Negative	17	71	45	71	13.7	(10.7–Inf)	17.1	(14.6–24.0)
Positive	7	29	18	29	8.6	(6.1–Inf)	14.3	(8.4–32.8)
Perineural invasion								
No	10	42	28	44	10.8	(6.1–Inf)	16.5	(11.2–34.5)
Yes	14	58	35	56	13.7	(10.7–Inf)	16.3	(13.4–21.5)
Perivascular invasion								

Characteristic	Patients		Overall survival			
	Distal pancreatectomy alone		Chemoradiation		Distal pancreatectomy alone	
	N	%	N	%	Median	95% CI
No	18	75	49	78	13.1	(6.6–Inf)
Yes	6	25	14	22	11.0	(10.7–Inf)
					15.7	(12.0–23.2)
					18.8	(16.2–Inf)