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Resected pancreatic adenosquamous carcinoma: clinicopathologic review and evaluation of adjuvant chemotherapy and radiation in 38 patients

K. Ranh Voong, BA^a, Jon Davison, MD^c, Timothy M. Pawlik, MD^b, Manuel O. Uy, PhD^a, Charles C. Hsu, MD^a, Jordan Winter, MD^b, Ralph H. Hruban, MD^c, Daniel Laheru, MD^d, Sonali Rudra, MD^a, Michael J. Swartz, MD^a, Hari Nathan, MD^b, Barish H. Edil, MD^b, Richard Schulick, MD^b, John L. Cameron, MD^b, Christopher L. Wolfgang, MD^b, and Joseph M. Herman, MD, MSc^{a,*}

^aDepartment of Radiation Oncology and Molecular Radiation Sciences, The Sol Goldman Pancreatic Cancer Research Center, Johns Hopkins Hospital, Baltimore, MD 21231-6681, USA

^bDepartment of Surgery, The Sol Goldman Pancreatic Cancer Research Center, Johns Hopkins Hospital, Baltimore, MD 21231-6681, USA

^cDepartment of Pathology, The Sol Goldman Pancreatic Cancer Research Center, Johns Hopkins Hospital, Baltimore, MD 21231-6681, USA

^dDepartment of Medical Oncology, The Sol Goldman Pancreatic Cancer Research Center, Johns Hopkins Hospital, Baltimore, MD 21231-6681, USA

Summary

Pancreatic adenosquamous carcinoma is a rare morphological variant of pancreatic adenocarcinoma with an especially poor prognosis. The purpose of this study is to identify clinicopathologic features associated with prognosis, assess whether the percentage of squamous differentiation in pancreatic adenosquamous carcinoma is associated with an inferior prognosis, and examine the impact of adjuvant chemoradiation therapy on overall survival. Forty-five (1.2%) of 3651 patients who underwent pancreatic resection at the Johns Hopkins Hospital, Baltimore, MD, between 1986 and 2007 were identified with adenocarcinoma of the pancreas with any squamous differentiation. All pathologic specimens were re-reviewed. Statistical analyses were performed on the 38 patients amenable to adjuvant chemoradiation therapy for whom clinical outcome data could be obtained. Median age was 68 years (61% male). Sixty-one percent underwent pancreaticoduodenectomy. Median tumor size was 5.0 cm. Seventy-six percent of carcinomas were node positive, 37% were margin-positive resections, and 68% had 30% or more squamous differentiation. Median overall survival of the pancreatic adenosquamous carcinoma cohort was 10.9 months (range, 2.1–140.6 months; 95% confidence interval, 8.2–12.5 months). Adjuvant chemoradiation therapy was associated with superior overall survival in patients with pancreatic adenosquamous carcinoma ($P = .005$). Adjuvant chemoradiation therapy was associated with improved survival in patients with tumors 3 cm or larger and vascular or perineural invasion ($P = .02$, $.03$, $.02$, respectively). The proportion of squamous differentiation was not associated with median overall survival ($<30\%$ versus 30% , $P = .82$). Survival after pancreatic resection of pancreatic adenosquamous carcinoma is poor. Treatment with adjuvant chemoradiation therapy is

associated with improved survival. The proportion of squamous differentiation in resected pancreatic adenosquamous carcinoma specimens does not appear to impact overall survival.

Keywords

Chemoradiation; Adjuvant therapy; Pancreatic adenosquamous carcinoma

1. Introduction

Pancreatic adenocarcinoma is a highly aggressive cancer with a 1-year survival rate of 19% and a 5-year survival rate of 4% for unresectable patients [1]. For patients with resected adenocarcinoma, the median and 5-year survivals are only 17.9 months and 20%, respectively [2]. Pancreatic adenosquamous carcinoma (PASC) is a rare morphological subtype of pancreatic adenocarcinoma, which comprises only 1% to 4% of exocrine pancreatic malignancies [3-7]. Histologically, PASC of the pancreas is strictly defined as a neoplasm with 30% or more malignant squamous cell carcinoma mixed with ductal adenocarcinoma [8]. However, it is unknown whether the degree of squamous cell differentiation in PASC (eg, <30% versus ≥30%) is clinically relevant [6]. In fact, given the rarity of PASC, little is known about which prognostic factors are associated with PASC. In addition, the optimal management of these patients in the postoperative adjuvant period remains poorly defined. Only a few anecdotal studies regarding the efficacy of adjuvant chemotherapy and radiation treatment of PASC have been published [5,6,10,11].

The purpose of this study was to examine our single-center experience of patients with resected PASC, and to our knowledge, it is the largest single-center series to date. Specifically, we examined which clinicopathologic features were associated with prognosis after resection of PASC with particular attention to the potential prognostic importance of the degree of squamous cell component. In addition, we evaluated the impact of adjuvant chemoradiation therapy (CRT) on outcome of patients with PASC after surgical resection.

2. Materials and methods

After obtaining approval from the Johns Hopkins Institutional Review Board, the prospectively collected pathology database at Johns Hopkins Hospital (JHH), Baltimore, MD (September 2, 1986 to May 19, 2007), was searched for pancreatic carcinoma specimens reported to contain any amount of squamous differentiation. The search identified 45 patients with a diagnosis of adenocarcinoma with squamous differentiation. These 45 cases represented 1.2% of a total of 3651 patients who underwent pancreatic resection (pancreaticoduodenectomy [PD], distal or total pancreatectomy) for malignant or benign conditions during that same period. Excluded from final analysis were 2 patients found to have distant metastasis at surgical resection, 3 patients with very low survival months (<2 months), and 2 other patients who were lost to follow-up. The final study includes 38 patients for whom archival histopathologic material and clinical outcome data could be obtained.

Clinical data including demographics, operative details, adjuvant treatment, as well as outcome were collected. Data on preoperative characteristics including symptoms (eg, weight loss, abdominal pain, and jaundice), tobacco use, and comorbid conditions (eg, diabetes mellitus, hypertension, myocardial infarction, coronary artery disease, and chronic obstructive pulmonary disease) were collected. Other collected variables included intraoperative blood loss, units of blood transfused, length of hospital stay, and postoperative complications.

All available histologic slides were re-reviewed by a single pathologist (J. Davison). The proportion of squamous differentiation in the primary carcinoma was assessed using morphological criteria (including absence of gland lumen formation, mucin production, cell shape, quality of intercellular borders and cytoplasm, and the presence of keratinization). In certain cases, it was difficult to quantify the percentage of the carcinoma with squamous or glandular differentiation. Squamous differentiation most often occurred in poorly differentiated carcinomas, and the adenocarcinoma and squamous carcinoma components were usually admixed within the same section of the tumor. In such cases, a poorly differentiated component was determined to be either glandular (adenocarcinoma) or squamous based on whether glandular or squamous differentiation predominated in that region of the carcinoma that was sampled. Each section of the primary tumor was scored separately, and an overall estimate was based on the average, taking into account the amount of tumor on each slide.

The presence or absence of an “undifferentiated” component was also noted. Undifferentiated carcinoma was defined as a malignant epithelial neoplasm lacking identifiable histologic features of squamous or glandular differentiation [8]. The undifferentiated components of these neoplasms typically exhibited sarcomatoid features or were composed of sheets of discohesive, highly anaplastic cells. The presence or absence of perineural invasion, vascular invasion, and lymph node metastases were documented, as was whether the involvement was due to infiltration by the squamous component, glandular component, or both. An average of 10 slides (median, 9; range, 2-40) of carcinoma (including metastases) was reviewed for each case. Information about tumor size, the status of margins, as well as total lymph node counts was obtained from the original pathology reports and confirmed by review of the available slides. The current American Joint Committee on Cancer (AJCC) pathologic tumor stage was determined from slide review and a review of the original pathology report. Cases in which the uncinate (retroperitoneal) margin was determined to be positive were categorized as T4 lesions under the presumption that the tumor involved the superior mesenteric artery.

Details regarding adjuvant chemoradiation (CRT) were retrospectively collected. For patients with available chemotherapy detail, chemotherapeutic agents included 5-fluorouracil (5-FU), gemcitabine, and capecitabine. Patients who underwent CRT at JHH received 5-FU-based chemoradiation as previously described [2]. For patients with available radiotherapy detail, the median radiation dose was 5040 Gy (range, 4500-5000 Gy).

2.1. Statistical analysis

Survival was determined and verified using Cancer Center abstracting services and the Social Security Death Index. Statistical analyses were performed using JMP statistical software, version 8 (SAS Institute Inc., Cary, N.C.) [12]. Tests of differences between variables were performed using *t* tests, F tests, and χ^2 tests. For characteristics with individuals missing data, χ^2 tests were performed including only those with known status, as indicated. The primary outcome variable was median overall survival (OS) defined as the time from surgical resection of PASC to death. If the patient was still alive, the date of last follow-up was used as censored data. Survival curves were estimated using Kaplan-Meier techniques [13]. The proportion of individuals surviving up to 1, 2, and 5 years was calculated using life tables. Univariate analyses were performed on variables known to be prognostically important for pancreatic cancer as previously described [9,14].

3. Results

3.1. Patient and tumor characteristics

The median age at the time of surgery was 68 years (range, 43-84 years). Most of the patients (61%) were 65 years or older, 61% were male, and 87% were white. Abdominal pain, weight loss, and jaundice at presentation were reported in 68%, 53%, and 47% of patients, respectively. Fifty-five percent of patients had a history of hypertension, and 32% had a history of diabetes. Patients underwent a PD (61%), distal pancreatectomy (26%), or total pancreatectomy (13%). The overall patient characteristics are summarized in Table 1.

The median tumor size was 5 cm in diameter (range, 1.5-14.5 cm). Eighty-four percent of patients had tumors 3 cm or larger, and 55% had tumors involving the head of the pancreas. Histologically, 76% of the carcinomas were poorly differentiated, 13% had undifferentiated cellular components, and 37% were resected with a positive margin. Most of the patients (76%) had regional lymph node metastases. The median number of total lymph nodes positive for metastases was 2 (range, 0-8) of the median of 17 total nodes (range, 4-38) evaluated at the time of resection. Perineural and vascular invasion was seen in 87% and 82% of the specimens, respectively.

The percentage of the carcinoma exhibiting squamous differentiation ranged from 10% to 90%. Most of the specimens 26/38 (68%) met the proposed criteria of 30% or more squamous differentiation for the diagnosis of PASC. Representative pathologic features of PASC are shown in Figs. 1 and 2.

3.2. OS: clinical and pathologic prognostic factors

At a median follow-up of 9.6 months (range, 2.1-140.6 months), the median OS of patients undergoing resection for PASC was 10.9 months, with 1- and 2-year survival rates of 34% (13/38) and 11% (4/38), respectively (Fig. 3 and Tables 1 and 5). On univariate analyses, only adjuvant chemoradiation (CRT) was significantly associated with improved survival (Table 2, $P = .005$). Patients 65 years or older showed a trend toward shorter OS when compared with patients younger than 65 years (9.6 versus 12.8 months); however, this difference was not significant ($P = .06$). Other factors found to be prognostic in pancreatic adenocarcinoma such as tumor size, tumor differentiation, margin, and node status were not associated with OS in PASC (all $P > .05$), but the sample size evaluated here is small ($n = 38$). Similarly, other preoperative, intraoperative, and postoperative factors that have traditionally been prognostic in patients with resected pancreatic adenocarcinoma, such as estimated operative blood loss and postoperative stay, were not associated with survival in patients with PASC (all $P > .05$). In addition, type of surgery (PD versus distal/total, $P = .79$) and having tumor stage of T3 or higher ($P = .42$) were not predictive of survival in this sample set.

The proportion of squamous differentiation in the carcinoma (<30% versus ≥30%) did not influence survival (11.0 versus 10.1 months, $P = .82$). Similarly, when the proportion of squamous differentiation was evaluated as a continuous variable, squamous cell differentiation did not significantly influence survival ($P = .25$).

We evaluated whether or not the squamous component was more likely to exhibit aggressive pathologic features such as lymph node metastasis, perineural invasion, or vascular invasion. The squamous component was less likely than the glandular component of PASC to metastasize to lymph nodes (21/33 versus 33/33, $P = .001$ by the upper tailed t test). However, the squamous component was more likely to demonstrate vascular invasion ($n = 26$ versus 16, $P = .01$). There was no significant difference in the propensity of squamous and glandular components of PASC to invade perineural structures ($n = 26$ versus 24, $P = .$

41). Overall, the presence of lymph node metastases, vascular invasion, or perineural invasion was not predictive of survival (all $P > .05$). In addition, poorly differentiated or undifferentiated cellular components did not significantly influence OS ($P > .05$).

3.3. OS: adjuvant CRT versus no CRT

Fifty percent of patients received adjuvant CRT, 7.9% received gemcitabine chemotherapy alone, and the remainder (42.1%) had no documentation of receiving any adjuvant therapy (no CRT). Patients who received adjuvant CRT had clinicopathologic characteristics similar to patients who did not receive adjuvant CRT (no CRT and gemcitabine chemotherapy) (Table 3). Adjuvant CRT was associated with a statistically significant superior OS in patients with resected PASC ($P = .005$, Table 2 and Fig. 4). Excluding the patients known to receive chemotherapy alone, adjuvant CRT was still significantly associated with improved survival ($P = .009$).

Receiving adjuvant CRT after a PD (excluding distal and total pancreatectomy) was associated with a superior survival ($P = .004$). In terms of pathologic characteristics, adjuvant CRT was associated with improved survival in patients with PASC with tumor diameter 3 cm or larger ($P = .02$), poor differentiation ($P = .02$), lymph node, vascular or perineural invasion ($P = .003$, $.03$, and $.02$, respectively), and squamous component 30% or more ($P = .04$). Individuals with squamous invasion of lymph nodes, vasculature, and perineural structures benefited from adjuvant CRT ($P = .004$, $.03$, $.03$, respectively). Adjuvant CRT was not associated with improved survival in patients with significant undifferentiated components ($P = .35$) (Table 4).

Three (75%) of the 4 patients who survived longer than 2 years received adjuvant chemoradiation (Table 5). These patients survived from 29.3 months (6.5-cm tumor, margin positive, node negative), 69.3 months (3.5-cm tumor, margin negative, node negative), and 140.6 months (3-cm tumor, margin negative, node positive), respectively. The 2 longest survivors received 5-FU-based adjuvant chemoradiation and had smaller tumors compared with the median (5.0 cm). Of the patients who had documented PASC recurrence ($n = 8$), 88% developed metastatic disease in the lung or liver. There was one known local recurrence of PASC to the lateral wall of the stomach (outside the radiation field).

4. Discussion

4.1. OS and prognostic features

There have been several case reports and a few case series reporting on PASC [6,11,15-33]. To our knowledge, this study is the largest single institution study ($n = 38$) to specifically examine the impact of adjuvant chemoradiation on outcome of patients with resected PASC. We also evaluated whether the proportion of squamous differentiation in the carcinoma influenced prognosis and whether known prognostic factors for resected PASC are similar to pure pancreatic adenocarcinoma.

Patients with resected adenosquamous carcinoma in our series have a poor prognosis (median OS, 10.9 months) when compared with our published study on pure resected adenocarcinoma at the JHH (median survival, 17.9 months) [2]. Interestingly, factors known to be associated with worse prognosis in patients with pancreatic adenocarcinoma, such as lymph node metastasis and positive resection margin, were not predictive of survival in patients with PASC, which may be reflective of the small sample size of this series.

In assessing if the frequency of prognostic factors in PASC ($n = 38$) differed from that of pancreatic adenocarcinoma ($n = 616$) at the JHH, the median size of resected adenosquamous carcinoma of the pancreas (median, 5.0 cm; range, 1.5-14.5) was found to

be comparatively larger than that of resected pancreatic adenocarcinoma (median, 3.0 cm; range, 0.1-14.0). However, the frequencies of other prognostic variables such as lymph node and margin positivity are similar between PASC and pancreatic adenocarcinoma (76% versus 80.2% and 37% versus 44.6%, respectively). TNM staging could not be compared between resected PASC and adenocarcinoma because the AJCC staging manual was updated in 2002, and therefore staging was inconsistent through the Johns Hopkins database. Thus, PASC appears to be discovered at a larger size but does not appear to present at a more advanced stage in terms of margin status and lymph node metastases.

PASC in this series demonstrated many aggressive pathologic characteristics: 76% of resections were node positive, 76% were poorly differentiated, 84% measured 3 cm or larger, and most resections demonstrated vascular (82%) or perineural invasion (87%). Similar high rates of lymph node metastases (92%, $n = 12$, and 83%, $n = 5$) have been reported by others [5,29]. Although the series reported by Smoot et al [28] discussed a high percentage of cases with perineural invasion (100%) in resected carcinomas ($n = 12$), they demonstrated comparatively smaller proportion of lymph node metastases and vascular invasion (33% and 17%, respectively). Further investigation would be needed to delineate whether PASC has inherently aggressive behavior similar to adenosquamous versus adenocarcinoma in other organs.

Although dismal, the median OS of 10.9 months reported in our small series of 38 patients who all underwent pancreatic resection with curative intent is, as expected, higher than the survival (range, 4.4-5.8 months) reported in other series of unresectable patients with PASC [5-7,32]. One series ($n = 12$ with resection, total $n = 23$) cited survival of 14.4 months for R0, 8 months for R1, and 4.8 months for palliative resections [28]. A series reviewing the English literature (1980-2007) noted a median survival of 6.8 months for 39 patients who underwent surgical resection of PASC [30]. None of these series specifically analyzed the effect of adjuvant CRT on OS for patients undergoing resection at a single institution.

4.2. Significance of the amount of squamous differentiation

The proportion of squamous cell differentiation necessary to diagnose PASC has been somewhat arbitrarily set at 30% or more of the carcinoma [5,6,8]. However, others have argued against this strict pathologic definition for PASC [6,33]. These latter authors claim that evaluating the proportion of squamous cell component in tumor specimens is too subjective and argue that pancreatic adenocarcinomas with any degree of squamous differentiation should be diagnosed as adenosquamous carcinoma. Given that adenosquamous carcinoma of the pancreas is regarded as a distinct entity not only because of its histologic features but also because of its aggressive clinical behavior, it would be of interest to assess whether or not a larger proportion of squamous differentiation is associated with poor outcome, and thus, if a valid, cutoff can be established to define this clinicopathologic entity. In our study, a single pathologist used a pragmatic approach likely to be used in standard clinical practice to assess the proportion of the carcinoma exhibiting squamous differentiation. In our analysis of these results, subdividing carcinomas into those with less than 30% ($n = 12$) versus those with greater or equal to 30% ($n = 26$) squamous differentiation was not predictive of survival. Hence, our data do not support the current cutoff of 30% squamous differentiation in the definition of adenosquamous carcinoma.

The presence of any squamous component in pancreatic carcinoma appears to portend a poor prognosis relative to historic controls treated at our institution during the same period [2]. It is unclear if the poor outcome is due to the high proportion of patients having known poor prognostic factors or if stage for stage having a squamous component results in especially poor outcomes. Further studies are needed to assess whether any degree of

squamous differentiation in pancreatic adenocarcinoma is an independent adverse prognostic factor.

4.3. Adjuvant therapy

In our series, patients with resected PASC who received adjuvant chemoradiation had a significantly improved survival when compared with no CRT ($P = .005$). Furthermore, adjuvant CRT statistically improved survival in resected patients with PASC with prognostic factors that were demonstrated to be poor in pancreatic adenocarcinoma. Pathologic prognostic factors include larger tumor size of 3 cm or larger, poor differentiation, and any perineural or vascular involvement ($P < .05$). CRT also statistically improved survival in patients with increased squamous percentage ($> 30\%$) and squamous invasion of lymph nodes, neural and vascular structures ($P < .05$).

Previous reports on adjuvant CRT in patients with resected PASC have been mostly anecdotal [5-7,10,11,28,29]. One case study noted a prolonged 40-month recurrence-free survival of a resected patient with PASC who underwent radical surgery, intraoperative radiation therapy, adjuvant chemotherapy, and external beam radiation [10]. Another clinicopathologic series ($n = 25$) suggested that adjuvant chemotherapy without radiation may have increased the duration of survival in patients with PASC after resection [6]. Of the 4 patients (Table 5) who lived longer than 2 years in our series, 75% received adjuvant CRT.

4.4. Study limitations

There are a number of limitations to this study. Given its retrospective nature, the details of adjuvant therapy and outcome could not be fully assessed for patients treated elsewhere after resection. After surgical resection, information on patterns of recurrence for each group was not available in most cases because they were often followed by their local oncologist. The effects of these potential biases on the outcome of this study are unknown. In addition, because of the rarity of the disease, this study is relatively small ($n = 38$) and may be underpowered to show specifically which patients are likely to benefit from adjuvant CRT and may preclude the detection of a small difference in prognostic features. However, inclusion of this series with other series could better delineate prognostic clinicopathologic risk factors and which patients may benefit from adjuvant chemoradiation.

4.5. Conclusions

Resected PASC is a rare malignancy that portends a worse prognosis compared with pure pancreatic adenocarcinoma treated at our institution. Within our relatively small group of patients, we could not demonstrate that the proportion of squamous differentiation ($< 30\%$ versus $> 30\%$) in these neoplasms had an impact on OS. This raises the possibility that even small amounts of squamous differentiation in pancreatic adenocarcinoma is associated with biologically aggressive behavior. Adjuvant CRT was associated with improved OS in our group of patients, suggesting that patients with this rare form of pancreatic adenocarcinoma could benefit clinically from the incorporation of adjuvant CRT into their treatment regimen post-curative resection.

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Fig. 1.
Adenosquamous carcinoma of the pancreas (PASC).

Fig. 2.
Squamous component of PASC within the lumen of a vessel.

Fig. 3.
OS after surgical resection for PASC.

Fig. 4.
OS after surgical resection for PASC by adjuvant therapy, $P = .005$.

Table 1**Baseline patient and tumor characteristics**

	n = 38
	No. (%)
<i>Characteristic</i>	
Age, median (range)	68 (43-84)
Age ≥ 65 y	23 (61)
Sex	
Male	23 (61)
Race	
White	33 (87)
Tobacco history	11 (29)
<i>Comorbid disease and presenting symptoms</i>	
Coronary artery disease	5 (13)
Chronic obstructive pulmonary disease	1 (3)
Diabetes mellitus	12 (32)
Hypertension	21 (55)
Weight loss at presentation	20 (53)
Abdominal pain	26 (68)
Jaundice	16 (47)
<i>Treatment</i>	
Surgery type	
PD	23 (61)
Distal pancreatectomy	10 (26)
Total pancreatectomy	5 (13)
Adjuvant therapy	
CRT	19 (50)
Observation/chemotherapy only	19 (50)
Surgical complications	24 (63)
<i>Tumor characteristics</i>	
Tumor location	
Head	21 (55)
Body/tail	15 (40)
Neck, body, tail	2 (5)
Tumor diameter (cm), median (range)	5 (1.5-14.5)
Tumor diameter ≥ 3 cm	32 (84)
T-stage T3/T4	32 (84)
Node positive	29 (76)
Margin positive	14 (37)
Any vascular invasion	31 (82)
Any perineural invasion	33 (87)
Poor differentiation	29 (76)

	n = 38
	No. (%)
Undifferentiated	5 (13)
Adenocarcinoma vascular invasion	16 (42)
Adenocarcinoma perineural invasion	24 (63)
Squamous vascular invasion	26 (68)
Squamous perineural invasion	26 (68)
Node positive (squamous) ^a	21 (64)
30% squamous component	26 (68)
<i>Survival</i>	
OS, median (95% confidence interval, range)	10.9 (8.2-12.5, 2.1-140.6)
<i>Survival</i>	
OS, mean (95% confidence interval)	17.9 (8.7-27.2)
1-y survival	13 (34)
2-y survival	4 (11)
5-y survival	2 (5)

^aSome tumor specimens not available or unable to determine specific pathologic category (n = 5). Missing data for node positive (squamous).

Table 2

Associations with OS by risk group

All patients	OS, median (95% confidence interval) (mo)		OS, log-rank test
	No	Yes	P
Age at surgery 65 y	12.8 (8.2-15.7)	9.6 (5.4-11.3)	.06
Male	9.5 (6.9-11.3)	11.0 (8.0-14.1)	.13
White	4.7 (2.3-12.5)	11.0 (8.2-12.8)	.21
Tobacco history	11.0 (8.2-122.3)	8.3 (2.5-14.1)	.26
Adjuvant chemoradiation	8.6 (55.4-10.9)	13.6 (10.0-16.1)	.005
Tumor diameter 3 cm	10.3 (3.8-12.8)	10.9 (8.2-11.7)	.37
PD	11.1 (3.8-13.1)	9.6 (7.0-12.8)	.79
Poor differentiation	11.0 (8.2-13.1)	10.1 (7.0-2.8)	.75
Undifferentiated	10.9 (8.2-11.7)	7.8 (2.1-14.1)	.41
Margin positive	11.0 (8.0-12.8)	10.4 (55.4-11.7)	.54
Lymph node positive	13.8 (2.3-29.3)	9.6 (7.6-12.5)	.18
T-stage T3/4	14.0 (2.3-18.9)	10.9 (8.2-12.5)	.42
Any vascular invasion	11.0 (8.2-29.3)	10.4 (7.6-12.8)	.25
Any perineural invasion	8.0 (5.4-9.0)	11.0 (8.2-12.8)	.13
Adenocarcinoma vascular invasion	10.1 (8.0-13.1)	11.1 (6.9-12.8)	.58
Adenocarcinoma perineural invasion	8.5 (2.6-14.1)	11.0 (8.2-12.8)	.62
Squamous vascular invasion	10.4 (8.2-12.4)	11.1 (7.0-13.1)	.68
Squamous perineural invasion	9.1 (3.8-10.8)	11.8 (8.2-13.1)	.53
Node positive (squamous) ^a	10.4 (2.5-16.1)	11.0 (8.2-12.8)	.78
30% squamous component	11.0 (3.8-12.5)	10.1 (7.6-13.1)	.82

^aSome tumor specimens not available or unable to determine specific pathologic category (n = 5). Missing data for node positive (squamous).

Table 3

Distribution of clinicopathologic features between no CRT and adjuvant CRT groups

	No adjuvant CRT, n = 19	Adjuvant CRT, n = 19	P
	No. (%)	No. (%)	
Demographic			
Age at surgery 65	14 (61)	9 (39)	.10
Male	10 (43)	13 (57)	.31
White	15 (45)	18 (55)	.14
Diabetes history	6 (50)	6 (50)	1.00
Hypertension history	11 (52)	10 (48)	.74
Weight loss at presentation	10 (50)	10 (50)	1.00
Treatment			
Surgery type			
PD	11 (48)	12 (52)	.73
Distal/total pancreatectomy	8 (53)	7 (47)	
Surgical complication	11 (48)	12 (52)	.74
Estimated blood loss			
<700 mL	4 (67)	2 (33)	.38
700 mL	6 (38)	10 (62)	
Missing	9 (56)	7 (44)	
Postoperative stay 9 d	10 (56)	8 (44)	.62
Tumor characteristics			
Tumor diameter 3 cm	14 (44)	18 (56)	.07
Differentiation			
Well/moderate	4 (44)	5 (56)	.70
Poor	15 (52)	14 (48)	
Undifferentiated			
No	18 (55)	15 (45)	.14
Yes	1 (20)	4 (80)	
Margin positive			
No	14 (58)	10 (42)	.18
Yes	5 (36)	9 (64)	
Node positive			
No	4 (44)	5 (56)	.70
Yes	15 (52)	14 (48)	
T-stage T3/T4			
No	2 (33)	4 (67)	.37
Yes	17 (53)	15 (47)	
Any vascular invasion			
No	3 (43)	4 (57)	.67
Yes	16 (52)	15 (48)	
Any perineural invasion			

	No adjuvant CRT, n = 19	Adjuvant CRT, n = 19	P
	No. (%)	No. (%)	
No	4 (80)	1 (20)	.14
Yes	15 (45)	18 (55)	
Adenocarcinoma vascular invasion			
No	10 (45)	12 (55)	.51
Yes	9 (56)	7 (44)	
Adenocarcinoma perineural invasion			
No	7 (50)	7 (50)	1.00
Yes	12 (50)	12 (50)	
Squamous vascular invasion			
No	5 (42)	7 (58)	.48
Yes	14 (54)	12 (46)	
Squamous perineural invasion			
No	7 (58)	5 (42)	.48
Yes	12 (46)	14 (54)	
Node positive (squamous)			
No	4 (33)	8 (67)	.37
Yes	12 (57)	9 (43)	
30% squamous component			
No	6 (50)	6 (50)	1.00
Yes	13 (50)	13 (50)	

Table 4

Adjuvant CRT and associations with OS (months) by risk group

	<u>OS, median (95% confidence interval) (mo)</u>		<i>P</i>
	No CRT	Adjuvant CRT	
Risk group			
Age at surgery 65 (n = 23)	7.4 (2.8-10.9)	10.4 (2.1-13.1)	.34
With diabetes history (n = 12)	6.9 (3.8-7.0)	10.7 (7.6-16.1)	.04
Treatment			
PD (n = 23)	7.5 (2.8-8.2)	14.6 (7.6-22.7)	.004
Tumor characteristics			
Tumor diameter 3 cm (n = 32)	8.5 (2.8-11.0)	12.0 (8.2-18.9)	.02
T-stage T3/4 (n = 32)	8.6 (6.9-11.1)	12.01 (7.6-15.7)	.05
Poor differentiation (n = 29)	7.5 (2.8-9.0)	13.6 (7.6-16.1)	.02
Undifferentiated (n = 5)	1.25	13.6 (2.1-14.1)	.35
Margin positive (n = 14)	6.8 (2.5-8.2)	12.0 (2.6-16.1)	.06
Node positive (n = 29)	8.6 (3.8-10.9)	11.6 (7.6-15.7)	.003
Any vascular invasion (n = 31)	7.5 (3.8-10.9)	11.6 (7.6-15.7)	.03
Any perineural invasion (n = 33)	8.6 (2.8-11.1)	13.6 (10.0-16.1)	.02
Node positive (squamous) (n = 21)	9.0 (5.4-11.1)	11.2 (2.1-14.1)	.004
30% squamous component (n = 26)	8.6 (2.8-10.9)	15.1 (7.6-22.8)	.04
Vascular invasion (squamous) (n = 26)	7.5 (2.8-10.9)	14.9 (2.6-16.1)	.03
Perineural invasion (squamous) (n = 26)	8.6 (2.5-11.1)	14.9 (7.6-18.9)	.03

Table 5

Clinicopathologic summary of patients with 2 years survival or more

Patient no.	Adjuvant CRT	Tumor size (cm)	Margin	Node	Survival (mo)
1	Yes	6.5	+	-	29.3
2	No	7.5	-	-	59.2
3	Yes	3.5	-	-	69.3
4	Yes	3.0	-	+	1.06