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Clinical Features and Outcome of Primary Pancreatic Lymphoma

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Abstract

Introduction—Primary pancreatic lymphoma (PPL) is a rare tumor that is often misdiagnosed. Clinicopathologic features, optimal therapy, and outcomes are not well defined. We reviewed our institutional experience with PPL.

Methods—Search of our institutional database identified that between 1987–2012, 21,760 patients with lymphoma and 11,286 patients with a primary pancreatic tumor were evaluated. There were 44 patients with pathologically confirmed PPL. Clinical data were obtained by chart review and survival distributions were estimated using the Kaplan–Meier method and compared using the log-rank test.

Results—At baseline, LDH was elevated in 55 % of the patients, CA 19-9 in 25 %, and CEA in 20 %. Imaging characteristics included large, unresectable tumors (67 %), and lymphadenopathy inferior to the renal vein (50 %). Twenty-three patients underwent surgery for resection (5), diagnosis (13), or palliation (5). Chemotherapy alone achieved a 75 % complete response rate. Eight patients experienced relapse, 88 % of which occurred at distant sites. Median overall survival was 6.1 years and 10-year disease-specific survival (DSS) was 69 %. Patients with a low risk International Prognostic Index (IPI) and those with a follicular histologic subtype demonstrated 5-year DSS of 100 %.

Conclusions—Chemotherapy for PPL results in a high complete response rate and long DSS, which is similar to nodal non-Hodgkin's lymphoma (NHL). A favorable outcome is expected for IPI low risk patients and follicular histologic subtype. Systemic therapy should generally be the

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initial therapy when the diagnosis is known. Prolonged follow up is recommended to detect relapses. Surgery alone should be reserved for non-curative intent (i.e. diagnostic or palliative).

Primary pancreatic lymphoma (PPL) has been estimated to account for 0.2 % of all primary tumors of the pancreas¹ and approximately 0.1 % of all malignant lymphomas.² Historically, variable criteria have been used to define PPL.^{3,4} However, there is now a standardized definition within the current World Health Organization (WHO) framework of primary extranodal lymphomas, which facilitates uniformity and precision.⁵ PPL is defined when the bulk of the disease is localized to the pancreas. Adjacent lymph node involvement and distant spread may exist but the primary clinical presentation is in the pancreas and therapy is targeted to this location.

Primary pancreatic lymphoma represents a diagnostic and therapeutic challenge due to its rarity, difficult anatomic location to access, clinical presentation that can mimic pancreatic ductal adenocarcinoma, and variety of histologic subtypes. Histologic subtype is a major prognostic factor in nodal and extranodal lymphoma. Furthermore, compared with nodal lymphomas, extranodal lymphomas may have an unique organ-related pattern of dissemination that requires a specific therapeutic approach. For example, the recommendation for primary testicular lymphoma is prophylactic irradiation to the contralateral testis to avoid up to a 40 % chance of relapse there.⁶⁻⁹ Another distinct relapse pattern of primary testicular lymphoma includes CNS involvement in 30 % of patients in the absence of using prophylactic brain radiation.

Primary pancreatic lymphoma has been described in multiple case reports,¹⁰ and a literature review in 2006 estimated that only 150 cases had been published.¹¹ There have been a few institutional series but none larger than 12 patients.^{3,12-14} A surveillance, epidemiology, and end results (SEER) report exists but lacks the details of therapy and outcome.¹⁵ Because of the limited experience at any single center, it has been difficult to define an optimal management approach for these tumors or to estimate survival. Some series have estimated poor survival and recommended a more aggressive approach focused on local therapy, such as surgery.³ Others have reported PPL to be more indolent, similar to pancreatic neuroendocrine carcinoma, and suggested that surgical resection should be rarely performed.^{12,14} Herein, we summarize our experience of 44 patients with PPL.

METHODS

Patients and Definitions

Approval was obtained from the Institutional Review Board. A search of our institutional cancer database showed that between 1987 and 2012 there were 21,760 patients with any lymphoma and 11,286 patients with a primary pancreatic tumor evaluated. PPL was identified in 45 patients. Review of the medical records was performed to verify the diagnosis of PPL as defined by the WHO criteria.⁵ One patient was found to have primary pancreatic follicular dendritic cell tumor and was excluded. All pathology reports at initial diagnosis were reviewed by an expert hematopathologist (JT-F) and all available pathology specimens ($n = 25$) were reviewed. Pathologic specimens included biopsies of primary

tumors, adjacent lymph nodes, or resected tumors. Tumor histologic subtypes were classified according to WHO definitions.¹⁶

Clinical information was obtained from the medical charts; however, five cases involved specimens sent to Memorial Sloan Kettering Cancer Center (MSKCC) solely for pathological review. Of these five patients, the treating physicians were able to provide complete survival information for one patient and vital status for another patient. Thus, 39 patients had clinical and treatment data, while 41 had survival information. Twenty-six patients had their pre-treatment cross-sectional staging imaging archived at our institution and these were reviewed by an expert pancreas radiologist (RKGD). The Ann Arbor stage, lymphoma International Prognostic Index (IPI), and Eastern Cooperative Oncology Group (ECOG) performance scale were verified in all cases.^{17,18} Tumor response was evaluated after the end of chemotherapy and designated according to the Cheson criteria¹⁹ and/or the medical record.

Data Analysis

Descriptive and comparative statistics were performed using Statistical Software for the Social Sciences (SPSS) version 21 (IBM Corporation, Armonk, NY, USA). Survival distributions were estimated from the time of diagnosis using the Kaplan–Meier method and compared with the log-rank test to determine factors associated with survival. Disease-specific survival (DSS) was defined as death from lymphoma, while patients who died of other causes were censored. An event for progression-free survival (PFS) was defined as death, distant metastasis, any relapse after complete surgical resection, or any relapse after complete radiological response. Patients without events were censored at last follow-up. A *p* value 0.05 was considered statistically significant.

RESULTS

Patient and Tumor Characteristics

Primary pancreatic lymphoma was identified in 44 patients, i.e. 0.2 % of all patients with any lymphoma and 0.4 % of all patients with any primary pancreatic tumor evaluated at our institution. Patient characteristics are summarized in Table 1. The median age at diagnosis was 62.5 years (range 15–85), while the majority of patients (55 %) were males and 75 % were Caucasian. Diagnosis was established by surgery in 50 % of the patients (36 % laparotomy, 14 % laparoscopy), percutaneous biopsy in 34 %, and endoscopic biopsy in 9 %. The median time between the onset of symptoms to diagnosis was 1 month. The most common presenting symptom was abdominal pain (67 %), followed by B symptoms (38 %), jaundice (33 %), and duodenal obstruction (26 %). Of the 15 patients with B symptoms, 13 were stage II, one was stage I, and one was stage III. Physical examination was unremarkable in most cases (76 %), but in 24 % an abdominal mass was palpated. Pretreatment laboratory workup demonstrated an elevated serum lactate dehydrogenase (LDH) in 55 % of the patients, while 25 % had an elevated carbohydrate antigen 19-9 (CA19-9) and 20 % had an elevated carcinoembryonic antigen (CEA). ECOG performance status was 0–1 in 67 % of patients.

Two-thirds of patients were deemed unresectable at presentation. Twenty-six patients had their computed tomography (CT) imaging stored at our institution. These were reviewed and the findings are summarized in Table 1. Tumors had a median size at diagnosis of 7.9 cm and were located in the head/uncinate of the pancreas in 54 % of patients. Lymphadenopathy inferior to the renal vein occurred in 50 % of cases. The majority of the tumors (90 %) were localized and well-circumscribed, and the epicenter of the tumor was within the pancreas in 71 % of patients. Representative imaging with pathological correlation is shown in electronic supplementary Figs. S1 and S2.

Table 2 demonstrates that the most common (77 %) histologic subtype was diffuse large B-cell lymphoma (DLBCL), followed by follicular lymphoma (14 %). Early-stage disease (stages I and II) was diagnosed in 84 % of patients, with only 8 % presenting with bone marrow involvement. The three patients with stage III had only mediastinal lymphadenopathy other than the pancreatic tumor. The only distant spread for all stage IV patients was bone marrow involvement. Stratification according to the IPI criteria revealed that only a minority (16 %) was high risk (IPI grades 4–5). Four of six patients with follicular lymphoma were alive at last follow-up; the fifth patient died 13 days after pancreaticoduodenectomy that was complicated by an anastomotic leak, and the sixth patient was lost to follow-up.

Treatment Type and Outcome

The initial treatment was chemotherapy alone in 25 patients (64 %), chemotherapy plus radiation in three patients (8 %), surgical resection plus chemotherapy in three patients (8 %), and surgical bypass followed by chemotherapy in five patients (13 %). Surgical resection alone was performed in two patients (5 %). Observation was used in two patients (5 %) with follicular lymphoma (both alive at last follow-up after 4 and 5 years). Table 3 lists the response rates for those patients who received chemotherapy. Seven different chemotherapy regimens were administered. All regimens were doxorubicin-based, with the exception of one patient who received mitoxantrone, etoposide, cytarabine (MEC). Of those treated with chemotherapy without surgical resection, 21 (75 %) had a complete radiologic response, four (14 %) had a partial response, and three (11 %) had stable disease.

Twenty-three patients underwent a surgical procedure for resection (five patients, 22 %), diagnosis alone (13 patients, 56 %), or palliation (five patients, 22 %). Four patients underwent pancreatic resection (three pancreaticoduodenectomy, one distal pancreatectomy) for a presumed diagnosis of adenocarcinoma. In order to prevent infection before an autologous stem cell transplant, a distal pancreatectomy was performed in the fifth patient to remove necrotic tumor that had responded to the non-Hodgkin's lymphoma (NHL)-15 protocol and ICE (ifosfamide, carboplatin, etoposide) chemotherapy. The postoperative course of these five patients was complicated by one mortality, one pancreatic fistula, and one reoperation for bleeding, each in separate patients. Of the five patients who had surgical bypass, four underwent biliary bypass in order to treat obstructive jaundice before the initiation of chemotherapy. Another patient suffered from bowel obstruction secondary to erosion of the PPL into the jejunum and stomach, which was treated by gastrojejunostomy, and the patient then had a complete response from subsequent chemotherapy.

Survival Distributions

Complete data for overall survival (OS), PFS, and DSS were obtained for 41, 40, and 40 patients, respectively. The median follow-up for all patients was 34 months (range 0.4–289) and median follow-up for survivors was 66 months (range 1–289). Among the 44 PPL patients identified, 10 (23 %) died from their disease, 11 (25 %) died from causes unrelated to PPL, 19 (43 %) were alive at last follow-up, 1 (2 %) died from an unknown cause, and 3 (7 %) were lost to follow-up. The median OS of all patients was 6.1 years, and 5-year OS was 56 % (Fig. 1a). The 5, 10, and 20-year DSS was 75 % (CI 0.6–0.9), 69 % (CI 0.5–0.9), and 55 % (CI 0.3–0.8), respectively (Fig. 1a). It is noteworthy that there were few events in DSS after 2 years from diagnosis. Univariate analysis of factors associated with OS and DSS is shown in electronic supplementary Table S1. Patients younger than the median age had improved OS ($p = 0.02$; Fig. 1b). Low-risk patients (IPI 0–1) had longer DSS ($p = 0.05$; Fig. 1b).

Progression-free survival is depicted in Fig. 1c. Relapse occurred on follow-up CT in 8 of 34 patients after either complete surgical resection or chemotherapy with complete radiological response. One patient experienced local relapse at the pancreas 34 months after chemotherapy. The other seven patients developed distant relapses in the mediastinal, abdominal, and inguinal lymph nodes. Three of the eight patients had late relapses (range 3–7 years) and their initial IPIs were 0, 1, and 2. Survival profiles did not depend on stage, tumor location, or type of initial treatment (electronic supplementary Table S1, Fig. 1c). For the patients who underwent surgery as their initial therapy, there was a trend for them to do poorly, although the group was small. Their median PFS was 0.7 years versus 6.1 years for those who did not have surgery as an initial treatment ($p = 0.06$).

DISCUSSION

This study, which encompasses 25 years of experience at MSKCC, is the most comprehensive single-institution series to describe the clinical characteristics, treatment, and outcome of patients with PPL. The rarity of PPL makes it a diagnostic challenge. PPL can be easily mistaken for adenocarcinoma, which is the most frequent pancreatic cancer. Both tumors are diagnosed at a similar age²⁰ and can present with a well-circumscribed tumor and non-specific symptoms.²¹ Autoimmune pancreatitis is another diagnosis to consider that requires a different management approach.²² Common presenting features of PPL in this study included abdominal pain, weight loss, and jaundice—very similar to adenocarcinoma. However, laboratory workup can raise the possibility of PPL. The combination of an elevated LDH, normal CEA, and normal CA19-9 was frequent in our cohort as opposed to adenocarcinoma and autoimmune pancreatitis.²³ Additional characteristics of PPLs were large tumor size (median 7.9 cm), lymphadenopathy inferior to the renal vein, and bulky proximal pancreatic tumors without pancreatic duct dilatation.

On pathologic review, there were two predominant lymphoma subtypes—the DLBCL subtype (77 % of all patients) consisting of large neoplastic B cells with round nuclear contours, dispersed chromatin, several distinct nucleoli, and modest amounts of pale cytoplasm; and the follicular lymphoma subtype (14 % of all patients) characterized by a distinctly nodular proliferation with small, cleaved cells that resemble normal germinal

center B cells. This distribution pattern of histologic subtypes is similar to other extranodal lymphomas (testis, breast, and bone) but different from primary gastric lymphoma, in which 60 % are DLBCL and 38 % are mucosa-associated lymphoid tissue (MALT) lymphomas.^{24–27}

The response rate of patients treated solely with chemotherapy was approximately 85 % CR/PR and 15 % SD/PD, which is similar to reported response rates of patients with nodal DLBCL treated with either CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) or R-CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone, rituximab).²⁸ Patients with PPL demonstrated survival estimates similar to nodal NHL,^{18,29,30} with a median OS of 6.1 years and a 10-year DSS of 69 %. In addition, a similar survival pattern (i.e. an early-event group within the first 2 years and a late-event group) was recently described in nodal NHL by Maurer et al.,³¹ who concluded that patients who achieve event-free status at 2 years have a subsequent OS equivalent to that of the age- and sex-matched general population. Low-risk PPL (IPI 0–1) correlated with DSS by univariate analysis and resulted in 100 % 5-year DSS. In addition, follicular histologic subtype demonstrated a 5-year DSS of 100 %.

High relapse rates are reported for extranodal NHL (up to 40 %).^{7,32} It is postulated that extranodal lymphomas are prone to arise in the presence of a chronic immunoinflammatory process, which results in high rates of contralateral paired organ involvement and relapses that involve the tissue type or organ of origin.⁷ The relapse pattern in PPL is different. Only one patient in this study relapsed in the pancreas, while 88 % of relapses occurred at distant sites. The majority of the relapses were early events (less than 2 years) and resulted in the early drop in DSS, which may reflect the aggressive biology of the patients with a higher IPI (Fig. 1b). Nevertheless, nearly 40 % of the relapses were late events (range 3–7 years), which is uncommon in most nodal and extranodal forms of NHL.^{31,33,34} However, the propensity of primary extranodal lymphomas with initial early-stage disease and favorable IPI to develop late relapses has been reported.³⁴ Follow-up surveillance with CT identified all eight relapses in this study. Therefore, radiologic follow-up is advisable to detect late recurrences.

Earlier reports and literature review of 122 patients^{3,13} demonstrated improved outcome for patients with PPL treated with surgery, and treatment algorithms advocated surgical resection and even debulking.¹³ Notably, the vast majority of these reports relate to the pre-rituximab era, when no clear outcome definitions were reported, and no series included more than 12 patients. Moreover, it has never been demonstrated that surgery alone ever cured PPL. A literature review by Koniaris et al.¹³ revealed only two patients who were treated with surgery alone without adjuvant systemic or radiation therapy. Neither of these patients survived more than 16 months. We found that surgery was associated with a median PFS of 0.7 years, versus 6.1 years for those who did not have surgery as an initial treatment, although the number of patients was small.

Although the present data are retrospective, a few generalizations are warranted. Selected patients with follicular PPL may be observed. Otherwise, we recommend systemic chemotherapy as the initial treatment for PPL (even when it is resectable), given the high

complete response rates and favorable survival with chemotherapy, the propensity for distant failures, and the lack of data to demonstrate cure with surgery alone. In patients discovered to have PPL after pancreatic resection, systemic therapy should generally be administered. A suggested management algorithm is presented in Fig. 2.

CONCLUSIONS

Primary pancreatic lymphoma is very rare and a high index of suspicion is necessary to make the diagnosis, which may be suggested by a high serum LDH and normal serum CA19-9 and CEA, large tumor size, and lymphadenopathy inferior to the renal vein. Chemotherapy for PPL results in a high complete response rate and long DSS, which is similar to nodal NHL. A favorable outcome is expected for follicular histologic subtype, IPI low-risk patients, and patients who are event free after 2 years. Systemic therapy should generally be the initial therapy when the diagnosis is known. Prolonged follow-up is recommended to detect relapses. Surgery alone should be reserved for non-curative intent (i.e. diagnostic or palliative).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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FIG. 1.

Outcomes in PPL. **a** Median overall survival of all patients was 6.1 years and 5-year overall survival was 56 %. DSS curve for all patients, which estimates 5-year, 10-year, and 20-year DSS as 75 % (CI: 0.6–0.9), 69.1 % (CI: 0.5–0.9), and 55.1 % (CI: 0.3–0.8), respectively. **b** Overall survival analysis by age groups and DSS analysis by IPI low (0 and 1) versus non low (2 to 5) risk groups. **c** Progression-free survival analysis of all patients and progression-free survival of patients stratified by initial treatment

FIG. 2.

Management algorithm for primary pancreatic lymphoma. 1 Suspected primary pancreatic lymphoma based on the following clinical characteristics: large tumor size, lymphadenopathy inferior to the renal vein, bulky proximal pancreatic tumors without pancreatic duct dilatation, and the combination of an elevated LDH, normal CEA, and normal CA19-9. 2 The diagnosis of lymphoma is based upon the evaluation of histologic and immunophenotypic studies (immunohistochemistry or flow cytometry) interpreted in the context of the clinical scenario. If diagnosis is inconclusive with the previous studies, then genetic studies should be followed (cytogenetic or mutation detection studies). 3 Combined-modality therapy consisting of combination chemotherapy plus radiation therapy. 4 Other treatment modalities may be considered (e.g. radiation therapy, bone marrow transplant, surgical resection after incomplete response to systemic therapy, endoscopic or percutaneous palliation). *EUS* endoscopic ultrasound, *CNB* core-needle biopsy, *LDH* lactate dehydrogenase, *CEA* carcinoembryonic antigen, *CA19-9* carbohydrate antigen 19-9, *PPL* primary pancreatic lymphoma

TABLE 1

Patient characteristics (*n* = 44)

Clinical characteristic	Value
Age, years	62.5 (15–85)
Ethnicity	
Asian	2 (4 %)
African American	3 (7 %)
Caucasian	33 (75 %)
Unknown	6 (14 %)
Sex	
Female	20 (45 %)
Male	24 (55 %)
Diagnostic method	
Surgery	
Diagnostic laparoscopy	6 (14 %)
Exploratory laparotomy	16 (36 %)
Percutaneous biopsy	15 (34 %)
Esophagogastroduodenoscopy	3 (7 %)
Mediastinoscopy	1 (2 %)
Not recorded	3 (7 %)
Diagnosis period	
Before 1996	8 (18 %)
After 1996	36 (82 %)
Presenting symptoms ^a	
Abdominal pain	26 (67 %)
B symptoms (fever, night sweats, and weight loss)	15 (38 %)
Jaundice	13 (33 %)
Duodenal obstruction	10 (26 %)
Duration of presenting symptoms ^a	1 month (2 days–1 year)
Physical examination ^a	
Epigastric mass	7 (18 %)
LUQ mass	2 (5 %)
Unremarkable	28 (72 %)
Not recorded	2 (5 %)
Baseline laboratory values ^b	
LDH, units/L	243 (166–1,179)
LDH > 246 units/L (%)	55 %
CA19-9, units/ml	15 (0.5–125)
CA19-9 > 40 units/ml (%)	25 %
CEA, ng/ml	2.6 (0.5–6.7)
CEA > 5 ng/ml (%)	20 %

Clinical characteristic	Value
Calcium, mg/dl	9.4 (7.7–10.6)
Uric acid, mg/dl	4 (1.8–8.5)
Pre-treatment CT characteristics ^c	
Size, mm	79 (24–139)
Pancreatitis-like ^d	1 (5 %)
Morphologic pattern ^e	
Localized	19 (90 %)
Diffuse	2 (10 %)
Epicenter of tumor	
Pancreas	15 (71 %)
Retroperitoneum	6 (29 %)
Peripancreatic lymphadenopathy	13 (65 %)
Lymphadenopathy below the renal vein	10 (50 %)
Bulky proximal tumor without pancreatic duct dilatation	7 (33 %)
Resectable at diagnosis	34 % (11 of 32)
ECOG performance status 2	33 %

Continuous variables are expressed as median (range). Categorical variables are expressed as number of cases (%)

^a In these categories, we excluded five patients who were only consulted for pathology

^b Laboratory values were available in the following numbers of patients: LDH (33), CA19-9 (12), CEA (10), calcium (30), uric acid (20)

^c Twenty-six patients had CT imaging stored at our institution and 21 included CT that enabled complete re-evaluation. Size was re-evaluated for 26 patients, and other variables were re-evaluated for 21 patients

^d Pancreatitis-like radiological presentation included peripancreatic inflammatory fat stranding

^e Localized pattern: well-circumscribed tumor; diffuse pattern: diffuse enlargement infiltrating or replacing most of the pancreatic gland

TABLE 2

Pretreatment tumor characteristics

Characteristic	N (%)	Median follow-up (range) [months]	5-year DSS (%)
Bone marrow involvement	3 (8)	–	–
Lymphoma subtype			
Diffuse large B cell	34 (77)	28.7 (1–289)	75
Follicular lymphoma	6 (14)	61.7 (0.4–170)	100
Malignant lymphoma, lymphocytic, well differentiated, NOS	3 (7)	–	–
Burkitt's lymphoma	1 (2)	–	–
Location ^a			
Head and uncinate	22 (50)	27.1 (0.4–289)	75
Tail and body	22 (50)	34 (8–241)	74
Clinical stage (Ann Arbor)			
Early (84 %)			
I	8 (20)	32.1 (0.4–165)	80
II	25 (64)	61.7 (1–289)	80
Late (16 %)			
III	3 (8)	19.7 (10–34)	33
IV	3 (8)	34 (21–170)	67
IPI			
Low risk (0–1)	15 (40)	66 (1–241)	100
High risk (4–5)	6 (16)	21.8 (11–76)	50

Continuous variables presented as median with range.

Categorical variables presented as number of cases (%)

Survival and follow-up were calculated for groups of five or more patients

All calculations were performed for the 39 patients with clinical evaluation except the lymphoma subtype, which was analyzed for all patients, and the

International Prognostic Index, which was recorded for 38 patients

DSS disease-specific survival, IPI International Prognostic Index, NOS not otherwise specified

^aOverlapping location was counted as head and uncinate

TABLE 3

Characteristics of initial treatment ($n = 39$)

Initial treatment	N (%)	Radiologic response ^a	Median follow-up (range) [months]	5-year DSS (%)
Chemotherapy alone ^b				
Any regimen	25 (64)	PR = 14 %, CR = 72 %, SD = 14 %, PD = none	51 (1.1–289)	73
R-CHOP	14 (36)	PR = 15 %, CR = 70 %, SD = 15 %, PD = none	49 (9–102)	70
CHOP	4 (10)	–	–	–
Research protocols	2	–	–	–
ProMACE-CytaBOM	1	–	–	–
MEC	1	–	–	–
McGarth protocol	1	–	–	–
Surgical bypass+chemotherapy	5 (13)	PR = none, CR = 100 %, SD = none, PD = none	164.8 (8–241)	100
Chemotherapy+radiation ^c	3 (8)	–	–	–
Surgical resection+chemotherapy ^d	3 (8)	–	–	–
Surgical resection alone ^e	2 (5)	–	–	–
Observation alone (follicular lymphoma)	2 (5)	–	–	–

Continuous variables presented as median with range. Categorical variables presented as number of cases (%)

Survival, follow-up, and response were calculated for groups of five or more patients

CHOP cyclophosphamide, doxorubicin, vincristine, prednisone; *R-CHOP* cyclophosphamide, doxorubicin, vincristine, prednisone, rituximab; *ProMACE-CytaBOM* prednisone, doxorubicin, cyclophosphamide, etoposide, cytarabine, bleomycin, Oncovin® (vincristine), methotrexate, leucovorin; *MEC* mitoxantrone, etoposide, cytarabine; *McGarth protocol* cyclophosphamide, doxorubicin, vincristine, cytarabine, methotrexate, leucovorin, filgrastin

^aRadiological response was not recorded for five patients

^bRegimen type was not recorded for two patients treated with chemotherapy

^cOne patient who underwent surgical bypass received chemotherapy and radiation (counted in both rows)

^dPatient outcomes were: alive with disease after 85 months, dead of disease after 23 months, and no evidence of disease after 34 months

^eOne patient died 13 days after pancreaticoduodenectomy and the other was not able to tolerate adjuvant chemotherapy and died 8 months after pancreaticoduodenectomy