ORIGINAL ARTICLE

Prognostic impact of perineural invasion following pancreatoduodenectomy with lymphadenectomy for ampullary carcinoma

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Running Head: Prognostic factors for ampullary carcinoma

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ABSTRACT

Purpose: The aim of this study was to identify prognostic factors in patients undergoing pancreatoduodenectomy with lymphadenectomy for ampullary carcinoma.

Methods: The records of 46 consecutive patients with ampullary carcinoma who underwent pancreatoduodenectomy from 1988 through 2006 were retrospectively reviewed.

Results: A 98% rate of potentially curative (R0) resection was achieved. There was no 30-day mortality. Overall 5-year survival rate was 64%. Univariate analysis revealed that T3 and T4 tumor (ie, pancreatic parenchymal invasion) (P<0.001), lymph node metastasis (P=0.01), and perineural invasion (P<0.001) were significant predictors of poor prognosis. Furthermore, perineural invasion was found to be a significant independent predictor of poor prognosis by multivariate analysis (P=0.024).

Conclusions: Pancreatoduodenectomy with lymphadenectomy for ampullary carcinoma is a safe surgical procedure with an acceptable cure rate. The presence of perineural invasion may be useful for predicting poor prognosis in patients with ampullary carcinoma who undergo potentially curative resection.

Key Words: ampullary carcinoma, prognostic factor, perineural invasion, pancreatoduodenectomy

INTRODUCTION

Ampullary carcinoma is an uncommon type of periampullary tumor with a more favorable prognosis than other tumors arising in this location.(1, 2) The improved prognosis of this condition compared to pancreatic or biliary adenocarcinomas is thought to result in part from its higher rate of resectability, which can be achieved in over 80% of cases.(1, 3, 4) However, some patients eventually succumb to the disease, with 5-year survival rates following resection ranging from 38% to 67%.(1, 3-9) Many predictive factors have been reported to influence survival following ampullary carcinoma resection, including depth of tumor infiltration,(5, 7, 9, 10) lymph node metastasis,(1, 4, 6, 9-12) TNM stage,(5, 8) pancreatic invasion,(4, 12) and perineural invasion.(13, 14) Identification of predictors of failure and survival following potentially curative resection should enable selection of candidates for adjuvant treatment. The objectives of this single-center review were to determine the cure rate of patients who underwent pancreatoduodenectomy with standard regional lymphadenectomy for ampullary carcinoma and to identify which clinicopathologic variables may be associated with long-term survival in this patient population.

METHODS

Patient Population

We retrospectively reviewed 46 consecutive patients who

underwent pancreatoduodenectomy for ampullary carcinoma between January 1988 and December 2006 at the Department of Surgery, Hiroshima University Hospital. All patients underwent surgery to achieve cure and had a confirmed preoperative pathological diagnosis. All patients were Japanese, and included 27 men and 19 women of median age 69 (range, 22 to 82) years.

Operative Procedures

Pylorus-preserving pancreatoduodenectomy was performed for 39 patients and conventional Whipple's procedure was performed for 7 patients. All 46 patients underwent pancreatoduodenectomy with standard regional lymphadenectomy, with dissection of lymph nodes in the peripancreatic area, lower hepatoduodenal ligament, and along the right lateral aspect of the superior mesenteric artery and vein. However, aorto-caval nodes (celiac artery to inferior mesenteric artery) were dissected only when visibly swollen. Reconstruction was performed with pancreaticogastrostomy, hepaticojejunostomy, and duodenojejunostomy or gastrojejunostomy. The surgery was performed by a single team of experienced hepatobiliary-pancreatic surgeons during the 18-year study period.

Pathological Investigations

All resected specimens were examined pathologically with hematoxylin and eosin staining. The tumors were classified as papillary adenocarcinoma, tubular adenocarcinoma, or others.

Pancreatic parenchymal invasion, duodenal invasion, perineural invasion, and lymph node metastasis were determined through pathological examination. Tumor depth (T) and nodal status (N) were determined using standard TNM classification.(15) Regional lymph nodes used for nodal status determination included the anterior and posterior pancreaticoduodenal nodes, those in the lower hepatoduodenal ligament, and those along the right lateral aspect of the superior mesenteric artery and vein.(16)

Survival

Patients were followed regularly in outpatient clinics by undergoing computed tomography every 6 months for 5 years after surgery. Information on outcomes more than 5 years after surgery was collected by telephone or personal interview. If a patient died, the duration of survival after surgery and the cause of death were recorded. For surviving patients, postoperative survival time and status of recurrence were recorded. Disease-specific survival analyses with respect to three clinical factors (age, surgical procedure, and blood transfusion) and six pathological factors (tumor size, gross appearance, histological type, T score, N score, and perineural invasion) were performed using univariate and multivariate methods.

Statistical Analysis

Survival curves were estimated by the Kaplan-Meier method, and statistical differences among groups were detected by

log-rank test. Factors found to be statistically significant by univariate analysis were subjected to multivariate analysis with Cox proportional hazards model. *P* values <0.05 were considered to be statistically significant.

RESULTS

Operative Results

The median operative time was 320 minutes (range, 230-500 minutes). Median estimated blood loss was 1,220 g (range, 150-5,980 g). Of the 46 patients, 14 (30%) required perioperative blood transfusion. There was no 30-day mortality. Overall morbidity was 37% (17 of 46 patients). Delayed gastric emptying was the most common complication (n=6; 13%), followed by surgical site infection (n=5; 11%), pancreatic fistula (n=3; 7%), pneumonia (n=2; 4%), enteritis (n=2, 4%), bile leakage (n=1; 2%), and chylous ascites (n=1; 2%)(Table 1). None of the patients required subsequent surgery.

Pathological Findings

The median size of resected ampullary carcinomas was 1.9 cm (range, 0.5-6.2 cm). Gross tumor appearance was protruding type in 35 patients and ulcerating type in 11 patients. Tumor types included 32 tubular adenocarcinomas, 10 papillary adenocarcinomas, 2 mucinous adenocarcinomas and 2 others. Pathologically, pancreatic parenchymal invasion and duodenal invasion were identified in 14 and 20 patients, respectively. Thirty-two patients had T1 or T2 tumors, while fourteen had T3

or T4 tumors. The median number of resected lymph nodes was 20 (range, 5-107). Fifteen patients (33%) had lymph node metastasis. The lymph nodes in the peripancreatic area were most frequently involved, followed by nodes surrounding the superior mesenteric artery and nodes in the lower hepatoduodenal ligament. Perineural invasion was pathologically identified in 15 patients. Tumor staging was performed according to TNM criteria;(15) there were 22 stage IA tumors, 4 stage IB tumors, 5 stage IIA tumors, and 15 stage IIB tumors. Only 1 patient had pathologically tumor-positive surgical margins; thus, a 98% rate of potentially curative (R0) resection was achieved.

Survival Outcomes

The median follow-up time was 86 months. The estimated overall 5-year survival rate for the 46 patients was 64% (Figure 1). Recurrent disease occurred in 11 patients. Sites and nature of recurrence included liver metastases (n=6), peritoneal dissemination (n=3), and local disease (n=2). Eighteen patients survived for more than 5 years after surgery, while fourteen patients died within 5 years. Of these 14 patients, 4 died of other disease, including 1 case each of primary lung carcinoma, renal cell carcinoma, gastric adenocarcinoma, and unknown sudden death with no evidence of recurrence. The estimated disease-specific 5-year survival rate for all 46 patients was 73% (Figure 2).

Univariate analysis revealed that T3 and T4 tumors ($P<0.001$), positive nodal status ($P=0.01$), and presence of perineural invasion ($P<0.001$) were significantly associated

with disease-specific survival (Table 1). Median survival for patients with T3 and T4 tumors, lymph node metastasis, and perineural invasion was 11.5, 12.4, and 10.6 months, respectively. However, only perineural invasion maintained a significantly independent association with disease-specific survival (P=0.024) on multivariate analysis (Table 2). The disease-specific 5-year survival rates of patients with or without perineural invasion were 26% and 94%, respectively (Figure 3).

DISCUSSION

In this single-center experience, we have demonstrated that a radical surgical approach to ampullary carcinomas including pancreatoduodenectomy with standard regional lymphadenectomy is both safe and effective for achieving long-term survival. The zero perioperative mortality in this series is consistent with other series recently reported in the literature.(5, 8, 12, 14) These series have been conducted during the last 20 years, a period characterized by significant advances in imaging technology, surgical technique, anesthesia, critical care, and interventional radiology.(17) Overall 5-year survival rates for patients following pancreatoduodenectomy for ampullary carcinoma ranges from 38% to 67%, with a trend toward improved survival in more recent studies.(1, 3, 4, 6, 8, 14) Our 5-year overall survival rate of 64% is consistent with these current reports from high-volume centers.(1, 3-8, 12, 14) Because our patients were treated with

an identical technique by a single team of experienced hepatobiliary-pancreatic surgeons during the last 18 years, this analysis may more accurately reflect the clinical outcome that can be expected using the current treatment. The high rate of R0 resection achieved with pancreatoduodenectomy with standard lymphadenectomy may make a contribution to improved survival.

Various clinicopathologic factors have been reported to influence long-term survival following pancreatoduodenectomy for ampullary carcinoma, including absence of intraoperative transfusion,(3) tumor size,(18) histological tumor differentiation,(19) surgical margin,(1, 20) depth of tumor infiltration,(5, 7, 9, 10) pancreatic parenchymal invasion,(4, 12) lymph node metastasis,(1, 4, 6, 9, 10, 12, 19) lymphatic invasion,(5, 12) and perineural invasion.(13, 14) In our univariate analysis, T1 and T2 tumors, which are defined by the absence of pancreatic parenchymal invasion, negative lymph node metastasis, and absence of perineural invasion, significantly predicted improved postoperative survival. In our multivariate analysis, only absence of perineural invasion maintained its status as an independent predictor of long-term survival.

Although perineural invasion has frequently been recognized as a characteristic feature and indicator of poor prognosis in pancreatic adenocarcinoma,(21-24) its relevance in ampullary carcinoma has been less well described. Only a few previous ampullary carcinoma series that underwent multivariate analysis included perineural invasion as a predictive factor for survival.(1, 10, 12-14) Thirty-three

percent of our patients had perineural invasion, which is more frequent than the 15% to 22% reported in other series. Nakai et al.(13) reported that the incidence of microperineural invasion using immunohistochemical staining (56%) was higher than that of perineural invasion using hematoxylin and eosin staining, and that microperineural invasion is a prognostic factor for ampullary carcinoma. Our series is consistent with a series reported by Duffy et al.(14) in which ampullary carcinoma patients with perineural invasion in resected specimens portended a poor prognosis following pancreatoduodenectomy with lymphadenectomy. Ampullary carcinoma with perineural invasion may have a similar prognosis as pancreatic adenocarcinoma, in which the majority of patients have perineural invasion. The use of adjuvant therapy in patients with perineural invasion of ampullary carcinoma should be evaluated as a possible means of improving survival following potentially curative resection.

Lymph node metastasis has been reported to be a poor prognostic factor for ampullary carcinoma by several authors.(1, 4, 6, 9, 10, 12, 19) In our series, nodal status was a prognostic factor by univariate analysis, but was not an independent prognostic factor by multivariate analysis. Thirty-three percent of our patients had lymph node involvement, which is similar to the 28% to 46% reported in other series.(1, 3, 4, 6, 7, 9, 10, 14) The 5-year survival rate of our patients with positive nodal status was 40%, which is higher than the 16% to 31% reported in other series, in which nodal status has been identified as a significant prognostic factor.(1, 4, 6, 9) In

our series, an appropriate number of regional lymph nodes (median, 20) were surgically dissected and examined by experienced pathologists for each specimen. Sites and nature of recurrence in patients with R0 resection included 6 liver metastases, 3 peritoneal disseminations, and 1 local disease. The oncologic effect of identical and standard regional lymphadenectomy may explain why lymph node status was not an independent prognostic factor following surgery in this series.

The use of local resection for early ampullary carcinomas remains controversial. Some authors advocate local resection, i.e., ampullectomy for T1 lesions, with preoperative endoscopic ultrasound and intraoperative frozen section as the procedures of choice for identification of appropriate lesions.(4, 25, 26) Histologic evidence of invasion of the duodenal muscular layer has been shown to predict the presence of lymph node metastasis.(27) However, even endoscopic ultrasound can only accurately define the depth of invasion in 66% to 83% of cases.(28-30) Further, intraoperative frozen section examination cannot exclude infiltration of the margins of a local excision.(31) Moreover, recurrence rates as high as 60% to 75% following local resection for early ampullary carcinoma have been reported.(19, 20, 25, 31) In patients with a carcinoma in situ or a T1 carcinoma of the ampulla, 6% to 10% have lymph node involvement.(32) In our series, 1 patient with T1 moderately differentiated tubular adenocarcinoma had lymph node metastasis in the posterior pancreaticoduodenal nodes. Currently, standard pancreatoduodenectomy with lymphadenectomy can be safely performed with very low mortality

and impressive long-term survival for ampullary carcinoma; thus, ampullectomy is not a good alternative even in early ampullary carcinoma, due to its diagnostic and curability limitations.

In conclusion, Pancreatoduodenectomy with standard regional lymphadenectomy is a safe surgical procedure with acceptable long-term survival for ampullary carcinoma. The presence of perineural invasion following potential curative resection for ampullary carcinoma is a useful poor prognostic factor. The addition of adjuvant therapy to patients with perineural invasion should be evaluated as a possible means of improving long-term survival.

REFERENCES

1. Howe JR, Klimstra DS, Moccia RD, Conlon KC, Brennan MF. Factors predictive of survival in ampullary carcinoma. Ann Surg;228(1):87-94.1998.
2. Yeo CJ, Sohn TA, Cameron JL, Hruban RH, Lillemoe KD, Pitt HA. Periampullary adenocarcinoma: analysis of 5-year survivors. Ann Surg;227(6):821-831.1998.
3. Talamini MA, Moesinger RC, Pitt HA, Sohn TA, Hruban RH, Lillemoe KD, Yeo CJ, Cameron JL. Adenocarcinoma of the ampulla of Vater. A 28-year experience. Ann Surg;225(5):590-599; discussion 599-600.1997.
4. Beger HG, Treitschke F, Gansauge F, Harada N, Hiki N, Mattfeldt T. Tumor of the ampulla of Vater: experience with local or radical resection in 171 consecutively treated patients. Arch Surg;134(5):526-532.1999.
5. Todoroki T, Koike N, Morishita Y, Kawamoto T, Ohkohchi N, Shoda J, Fukuda Y, Takahashi H. Patterns and predictors of failure after curative resections of carcinoma of the ampulla of Vater. Ann Surg Oncol;10(10):1176-1183.2003.
6. Brown KM, Tompkins AJ, Yong S, Aranha GV, Shoup M. Pancreaticoduodenectomy is curative in the majority of patients with node-negative ampullary cancer. Arch Surg;140(6):529-532; discussion 532-523.2005.
7. Di Giorgio A, Alfieri S, Rotondi F, Prete F, Di Miceli D, Ridolfini MP, Rosa F, Covino M, Doglietto GB. Pancreatoduodenectomy for tumors of Vater's ampulla: report on 94 consecutive patients. World J

Surg;29(4):513-518.2005.

8. Kim RD, Kundhal PS, McGilvray ID, Cattral MS, Taylor B, Langer B, Grant DR, Zogopoulos G, Shah SA, Greig PD, Gallinger S. Predictors of failure after pancreaticoduodenectomy for ampullary carcinoma. J Am Coll Surg;202(1):112-119.2006.
9. Qiao QL, Zhao YG, Ye ML, Yang YM, Zhao JX, Huang YT, Wan YL. Carcinoma of the Ampulla of Vater: Factors Influencing Long-term Survival of 127 Patients with Resection. World J Surg;31(1):137-143.2007.
10. de Castro SM, van Heek NT, Kuhlmann KF, Busch OR, Offerhaus GJ, van Gulik TM, Obertop H, Gouma DJ. Surgical management of neoplasms of the ampulla of Vater: local resection or pancreatoduodenectomy and prognostic factors for survival. Surgery;136(5):994-1002.2004.
11. Roder JD, Schneider PM, Stein HJ, Siewert JR. Number of lymph node metastases is significantly associated with survival in patients with radically resected carcinoma of the ampulla of Vater. Br J Surg;82(12):1693-1696.1995.
12. Sakata J, Shirai Y, Wakai T, Yokoyama N, Sakata E, Akazawa K, Hatakeyama K. Number of positive lymph nodes independently affects long-term survival after resection in patients with ampullary carcinoma. Eur J Surg Oncol.2006.
13. Nakai T, Koh K, Kawabe T, Son E, Yoshikawa H, Yasutomi M. Importance of microperineural invasion as a prognostic factor in ampullary carcinoma. Br J Surg;84(10):1399-1401.1997.

14. Duffy JP, Hines OJ, Liu JH, Ko CY, Cortina G, Isacoff WH, Nguyen H, Leonardi M, Tompkins RK, Reber HA. Improved survival for adenocarcinoma of the ampulla of Vater: fifty-five consecutive resections. Arch Surg;138(9):941-948; discussion 948-950.2003.
15. Sobin LH, Wittekind C, editors. In: International Union Against Cancer (UICC): TNM Classification of Malignant Tumors, 6th edition. New York: Wiley-Liss; 2002.
16. Japanese Society of Biliary Surgery (JSBS). Classification of Biliary Tract Carcinoma, 2nd English edition. Tokyo: Kanehara and Co, Ltd; 2003.
17. Yeo CJ, Cameron JL, Sohn TA, Lillemoe KD, Pitt HA, Talamini MA, Hruban RH, Ord SE, Sauter PK, Coleman J, Zahurak ML, Grochow LB, Abrams RA. Six hundred fifty consecutive pancreaticoduodenectomies in the 1990s: pathology, complications, and outcomes. Ann Surg;226(3):248-257; discussion 257-260.1997.
18. Klempnauer J, Ridder GJ, Pichlmayr R. Prognostic factors after resection of ampullary carcinoma: multivariate survival analysis in comparison with ductal cancer of the pancreatic head. Br J Surg;82(12):1686-1691.1995.
19. Sperti C, Pasquali C, Piccoli A, Sernagiotto C, Pedrazzoli S. Radical resection for ampullary carcinoma: long-term results. Br J Surg;81(5):668-671.1994.
20. Allema JH, Reinders ME, van Gulik TM, van Leeuwen DJ, Verbeek PC, de Wit LT, Gouma DJ. Results of pancreaticoduodenectomy for ampullary carcinoma and analysis of prognostic factors for survival.

Surgery;117(3):247-253.1995.

21. Nagakawa T, Mori K, Nakano T, Kadoya M, Kobayashi H, Akiyama T, Kayahara M, Ohta T, Ueno K, Higashino Y, et al. Perineural invasion of carcinoma of the pancreas and biliary tract. Br J Surg;80(5):619-621.1993.
22. Nakao A, Harada A, Nonami T, Kaneko T, Takagi H. Clinical significance of carcinoma invasion of the extrapancreatic nerve plexus in pancreatic cancer. Pancreas;12(4):357-361.1996.
23. Takahashi T, Ishikura H, Motohara T, Okushiba S, Dohke M, Katoh H. Perineural invasion by ductal adenocarcinoma of the pancreas. J Surg Oncol;65(3):164-170.1997.
24. Hirai I, Kimura W, Ozawa K, Kudo S, Suto K, Kuzu H, Fuse A. Perineural invasion in pancreatic cancer. Pancreas;24(1):15-25.2002.
25. Branum GD, Pappas TN, Meyers WC. The management of tumors of the ampulla of Vater by local resection. Ann Surg;224(5):621-627.1996.
26. Clary BM, Tyler DS, Dematos P, Gottfried M, Pappas TN. Local ampullary resection with careful intraoperative frozen section evaluation for presumed benign ampullary neoplasms. Surgery;127(6):628-633.2000.
27. Yoon YS, Kim SW, Park SJ, Lee HS, Jang JY, Choi MG, Kim WH, Lee KU, Park YH. Clinicopathologic analysis of early ampullary cancers with a focus on the feasibility of ampullectomy. Ann Surg;242(1):92-100.2005.
28. Rattner DW, Fernandez-del Castillo C, Brugge WR, Warshaw AL. Defining the criteria for local resection of ampullary

neoplasms. Arch Surg;131(4):366-371.1996.

29. Cannon ME, Carpenter SL, Elta GH, Nostrant TT, Kochman ML, Ginsberg GG, Stotland B, Rosato EF, Morris JB, Eckhauser F, Scheiman JM. EUS compared with CT, magnetic resonance imaging, and angiography and the influence of biliary stenting on staging accuracy of ampullary neoplasms. Gastrointest Endosc;50(1):27-33.1999.
30. Shoup M, Hodul P, Aranha GV, Choe D, Olson M, Leya J, Losurdo J. Defining a role for endoscopic ultrasound in staging periampullary tumors. Am J Surg;179(6):453-456.2000.
31. Asbun HJ, Rossi RL, Munson JL. Local resection for ampullary tumors. Is there a place for it? Arch Surg;128(5):515-520.1993.
32. Klein P, Reingruber B, Kastl S, Dworak O, Hohenberger W. Is local excision of pT1-ampullary carcinomas justified? Eur J Surg Oncol;22(4):366-371.1996.

FIGURE LEGENDS

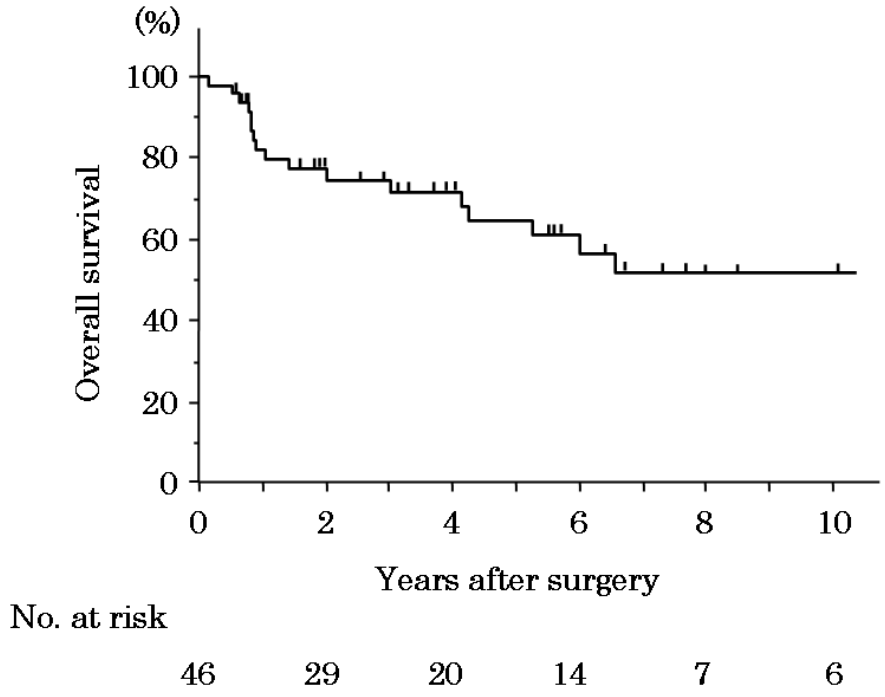


Figure 1.

Overall survival rate of patients with ampullary carcinoma who underwent pancreatoduodenectomy with standard regional lymphadenectomy.

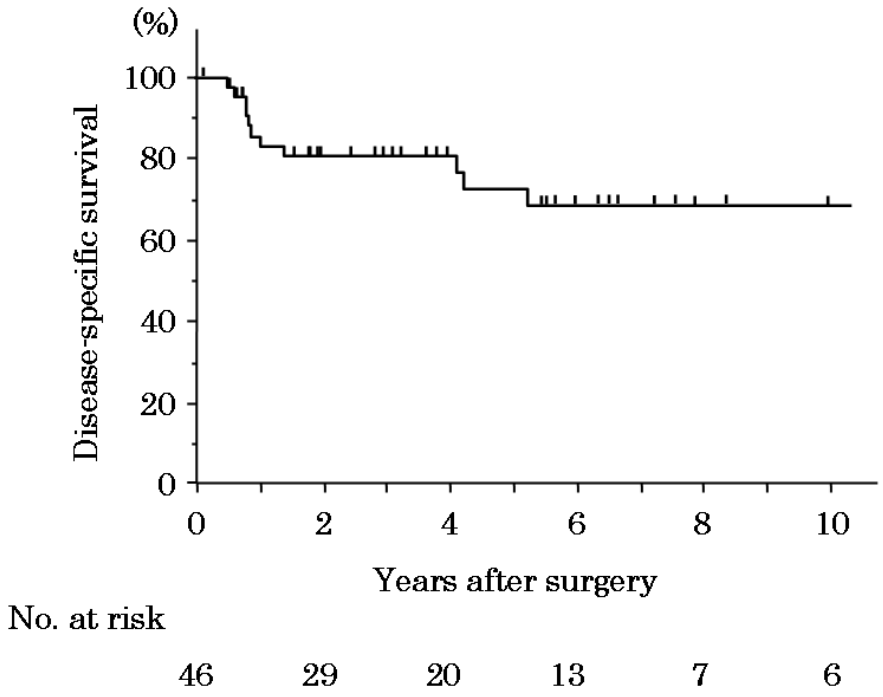
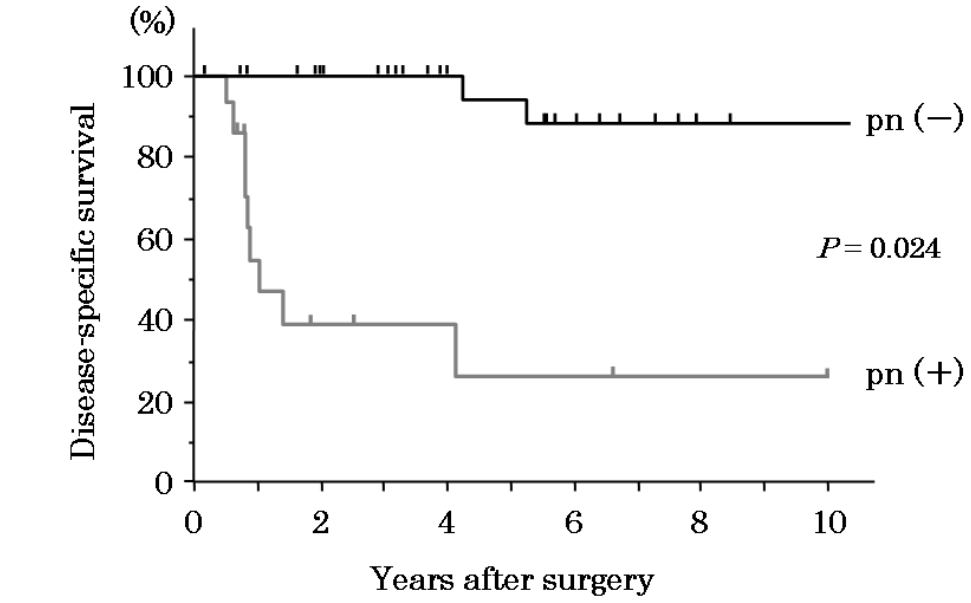


Figure 2.

Disease-specific survival rate of patients with ampullary carcinoma who underwent pancreatoduodenectomy with standard regional lymphadenectomy.



No. at risk

pn (−)	31	25	17	11	6	5
pn (+)	15	4	3	2	1	1

Figure 3.

Disease-specific survival rate of patients with and without perineural invasion of ampullary carcinoma who underwent pancreatoduodenectomy with standard regional lymphadenectomy.

pn: perineural invasion

Table 1. Demographic and operative parameters

Age, years	69 (22-82)
Operative time, minute	320 (230-500)
Estimated blood loss, g	1220 (150-5980)
Blood transfusion, U red cells	0 (0-17)
30-days mortality*	0 (0)
Overall morbidity*	17 (37)
Delayed gastric emptying*	6 (13)
Surgical site infection*	5 (11)
pancreatic fistula*	3 (7)
Pneumonia*	2 (4)
Enteritis*	2 (4)
biliary fistula*	1 (2)
chylous ascites*	1 (2)

All data are reported as median (range) unless otherwise indicated.
* Data are given as the number (percentage) of 46 patients.

Table 2. Univariate analysis of prognostic factors for patients following pancreatoduodenectomy for ampullary carcinoma

Factors	Number of patients	5-year survival rate(%)	*P* value
Clinical factors			
Age (years)			0.413
≦ 65	18	66	
> 65	28	80	
Operative procedure			0.310
Conventional PD	7	57	
Pylorus-preserving PD	39	75	
Blood transfusion			0.214
Yes	14	58	
No	32	80	
Pathological factors			
Tumor size (cm)			0.318
≦ 2	29	79	
> 2	17	61	
Gross appearance			0.142
Protruding type	35	77	
Ulcerating type	11	62	
Histological type			0.088
Tubular	32	65	
Papillary + others	14	92	
Tumor depth (T stage)			<0.001
T1 + T2	32	93	
T3 + T4	14	26	
Nodal status (N stage)			0.010
Positive	15	40	
Negative	31	84	
Perineural invasion			<0.001
Present	15	26	
Absent	31	94	

PD; pancreatoduodenectomy
P values are the results of log-rank tests.

Table 3. Multivariate analysis of prognostic factors for patients following pancreatoduodenectomy for ampullary carcinoma

Factors	Relative risk	95% CI	*P* value
Tumor depth (T stage)			
T1 + T2	1.00	0.10-3.03	0.501
T3 + T4	1.79		
Nodal status (N stage)			
Positive	1.92	0.56-6.58	0.299
Negative	1.00		
Perineural invasion			
Present	9.87	1.36-71.6	0.024
Absent	1.00		

CI; confidence interval
P values are the results of Cox proportional hazards models.