Original Paper

Evaluation of Surgical Resection for

Pancreatic Carcinoma at a Japanese Single Cancer Institute

Atsushi Nanashima[1], Syuuichi Tobinaga[1], Takafumi Abo[1], Kazuhiko Hatano[1],

Hiroaki Takeshita[1], Takashi Nonaka[1], Shigekazu Hidaka[1], Kenji Tanaka[1],

Masaki Kunizaki[1], Terumitsu Sawai[1], Toru Yasutake[1], Takeshi Nagayasu[1]

[1]Division of Surgical Oncology, Department of Translational Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, 1-7-1 Sakamoto, Nagasaki 852-8501, Japan

Running title: Resection in pancreatic carcinoma

Corresponding and reprint requests to: Atsushi Nanashima, M.D.

Division of Surgical Oncology, Department of Translational Medical Sciences,

Nagasaki University Graduate School of Biomedical Sciences,

1-7-1 Sakamoto, Nagasaki 852-8501, JAPAN

Tel.: +81-95-819-7304 , Fax: +81-95-819-7306

E-mail: a-nanasm@nagasaki-u.ac.jp

ABSTRACT

Background/Aims: Surgical resection is a radical treatment option for pancreatic carcinoma (PC); however, it is still difficult to cure and patient prognosis is poor at this stage.

Methodology: We examined the demographics, surgical records, and outcome in 64 patients with hilar PC undergoing surgical resection.

Results: Pancreatoduodenectomy (PD) was carried out in 48 patients, distal pancreatectomy (DP) in 14 and total pancreatectomy in two. Postoperative complications were observed in 18 patients (28%) but no hospital death. All stage I patients showed carcinoma in-situ of intraductal papillary mucinous carcinoma (IPMC). Postoperative adjuvant chemotherapy was performed in 15 patients (23%) using gemcitabine or S-1. Cancer recurrence was observed in 36 patients (56%) and 31 died of carcinoma. The 5-year cancer-free and overall survival rate was 12% and 14%, respectively. These survival rates were poor according to stage of tumor and survival, between Stage III, IVa and IVb were similar. CA19-9 level, morphological type, T category, lymph node metastasis, extrapancreatic nerve plexus invasion, retropancreatic tissue invasion, distal bile duct invasion, duodenal invasion and arterial system invasion were significant poor prognostic factors; however, portal vein system invasion was not significantly associated with prognosis. Cancer infiltration at bile duct cut-end and dissected peripancreatic tissue margin and presence of residual tumor showed a poor prognosis. Surgical prognosis in only non-invasive IPMC was satisfactory.

Conclusions: Radically extended surgical resection is necessary and newly effective adjuvant chemotherapy is a promising modality to improve patient survival in PC patients.

KEYWORDS: pancreatoduodenectomy, distal pancreatectomy, pancreatic carcinoma, curability

ABBREVIATIONS: Pancreatic carcinomas (PC), pancreatoduodenectomy (PD), distal pancreatectomy (DP),

INTRODUCTION

Surgical resection is the only curable treatment for pancreatic carcinomas (PC) although the resection rate is still low at this stage (1). Concurrent extended pancreatic resection is often necessary to accomplish complete (R0) resections, which may improve patient prognosis (1-5). Resection of the nerve plexus around the pancreas or combined resection of portal vein maintains surgical curability in PC patients (6, 7). On the other hand, physical stress in patients is relatively high and postoperative morbidity and mortality rates are still not low (8). Therefore, the indication of operation for PC should be carefully decided. In recent years, chemotherapy for PC has become effective and patient prognosis has improved (9). In patients who underwent surgical resection, adjuvant chemotherapy showed a survival benefit (10). Thus, treatment results for PC have been recently changed. To estimate the present status regarding surgical treatments for PC at our institute, we examined our series of PC in 64 patients at a Japanese single cancer institute and discuss the clinical significance and problems in the present report.

METHODOLOGY

Patients

We experienced 111 patients with PC administrated in the Division of Surgical Oncology, Department of Translational Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences (NUGSBS) between 1994 and 2008. In these patients, 64 patients (58%) who could undergo surgical resections were analyzed in the present study.

In another 47 patients, highly advanced PC such as a local extension to the supra-mesenteric artery (SMA), peritoneal dissemination or distant metastasis were found and radical operation was avoided before or during operation. The study design was approved by the Human Ethics Review Board of our institution. Informed consent for data collection was obtained by each patient during this period. Anesthetic and patient data were retrieved in the NUGSBS database. Tumor stage and curability was followed by the *Classification of Pancreatic Carcinoma* (11).

Operative procedures and follow-up

Pancreaticoduodenectomy (PD) is a basic surgical option for PC located in the pancreatic head and distal pancreatectomy (DP) is selected for PC in the body or tail of pancreas. In cases where PC extended widely, total pancreatectomy was selected in 2 cases. Lymphadenectomy was basically performed in Group 2 lymph nodes and lymph nodes at the para-aortic lesion (station number 16a2 and 16b1). Extrapancreatic nerve plexus was also resected in half of the cases around the SMA. In case of PD, Child's intestinal reconstruction with end-to-side anastomosis of pancreatojejunostomy or pancreato-gastrostomy was routinely selected. In case of DP, pancreatic stump was closed by suturing in a fish mouth shape.

In case of tumor involvement to the portal vein or supra-mesenteric vein (SMV), splenic artery or vein, and common hepatic artery, radical operation was considered. When combined resection of the portal vein or SMV was performed, end-to-end

anastomosis of vessels or graft interposition using expanded polytetrafluoroethylene (ePTFE; Gore-Tex®, W. L. Gore & Associates, Inc., Newark, DE) artificial blood vessel was applied. In case vascular anastomosis was expected for more than 30 minutes, we used a passive veno-venous bypass from the SMV to umbilical portal vein of the liver using an antithrombogenic Anthron® bypass tube (Toray Industries, Tokyo, Japan). When arterial blood flow was preserved via SMA, gastroduodenal artery and the proper hepatic artery, the combined resection of the common hepatic artery or celiac axis with distal pancreatectomy is considered to be resected. Fibrin glue was used to prevent pancreatic fistula.

After discharge from the hospital, the patient status, laboratory data, and disease recurrence were carefully checked every 3 months. The minimum follow-up period after operation was 12 months in the present study.

RESULTS

Patients included 39 men and 25 women with a mean age of 68.5 ± 9.6 years (± SD, range, 47-87 years). These patients underwent PD in 48 patients (pylorus preserving PD in 18, PD in 25 and subtotal stomach-preserving PD in 5), DP in 14 and total pancreatectomy in two. Postoperative complications were observed in 18 patients (28%) including pancreatic fistula in 3, delayed gastric empty in 8, bile leak in one, biliary obstruction in 2, chyle fistula in one, liver abscess in one, pneumonia in one, and obstruction of gastro-jejunostomy in one. Hospital death was not observed.

Stage of tumor was I in 5, II in 13, III in 12, IVa in 21 and IVb in 13. All patients with stage I showed carcinoma in-situ of intraductal papillary mucinous neoplasm (IPMN). Positive cancer margin at pancreatic cut-end margin was observed in 4 patients (6%), at bile duct cut-end margin in one (2%), and at dissected peripancreatic tissue margin in 7 (11%). Postoperative adjuvant chemotherapy was performed in 15 patients (23%) including use of $1g/m^2$ of gemcitabine (Gemzar; Eli Lilly and Co., Indianapolis, IN) in 10 and 80mg of S-1 (TS-1®; Taiho pharmaceutical Co, Ltd., Tokyo, Japan) in 5.

Postoperative cancer recurrence was observed in 36 patients (56%), which included peritonitis carcinomatosa in 9 patients, liver metastasis in 20, local recurrence in 5, and lung metastasis in 2. Thirty-five patients (55%) died after operation, which included cancer-related death in 31 and other disease in 4.

Figures 1 and 2 show the cancer-free and overall survival after operation. Mean cancer-free survival time was 22 months, and 3- and 5-year cancer-free survival rate was

22% and 12%, respectively. Mean overall survival time was 29 months, and 3- and 5-year overall survival rate was 25% and 14%, respectively. By comparison with tumor stage, 3- and 5-year tumor-free survivals were significantly different between Stages (80% and 80% in I, 33% and 33% in II, 9% and 0% in III, 13% and 6% in IVa and 9% and 0% in IVb, p=0.009). Mean cancer-free survival time was significantly correlated with Stages (76 months in I, 32 in II, 11 in III, 13 in IVa and 10 in IVb, respectively). By comparison with tumor stage, 5-year cancer-related overall survival was also significantly different between stages (100% in I, 63% in II, 17% in III, 26% in IVa and 10% in IVb, p=0.005). Mean cancer-related overall survival time was significantly correlated with Stages (206 months in I, 55 in II, 22 in III, 23 in IVa and 13 in IVb, respectively). Between stage III, IVa and IVb, postoperative survival was similar. Table 1 shows the relationship between overall 5-year survival rate and clinical parameters. CA19-9 level was significantly related to poor survival rate (p<0.05). Cystic or ductectatic type tumor showed better survival rate compared to nodular or infiltrative type (p<0.05). Table 2 shows the relationship between overall 5-year survival rate and pathological parameters. Higher T category, lymph node metastasis, non-invasive IPMC, extrapancreatic nerve plexus invasion, retropancreatic tissue invasion, distal bile duct invasion, duodenal invasion and arterial system invasion were significantly associated with poor survival. Portal vein system invasion was not significantly associated with prognosis. Cancer infiltration at bile duct cut-end margin and dissected peripancreatic tissue margin showed poor prognosis. By comparison between classification of lymph node dissection, degree of

dissection significantly correlated with poor prognosis. Presence of residual tumor tended

to show poor outcomes but was not significantly different.

DISCUSSION

Recently, aggressive surgical exploration with or without vascular resections for PC is usually performed and survival has been remarkably improved (1-7, 12). As the techniques and perioperative management have remarkably improved, we have actively performed extended resections for complete tumor resections (R0) during the last 15 years as well. Based on previous reports, the usefulness of R0 resection for PC has been reported in recent years (1-5).

In our series, the mean age of PC patients was similar to that in other reports (11, 12) and, as a modern trend, many patients were older than 70 years. Other reports showed that elderly patients over 80 years can also undergo this major surgery if the patient has no serious complications and a strong performance status (13). Our series included 7 patients over 80 years, and they had good operative courses. With respect to general conditions before surgery, only a few patients did not undergo radical operation due to severe chronic respiratory disorder using home oxygen treatment, accompanying multi-organ dysfunctions or senile dementia. Two patients undergoing hemodialysis may have had PD with good outcomes. Preoperative examinations for PC and its extension have been dramatically improved such as advanced computed tomography or magnetic resonance image, endoscopic retrograde pancreatography and associated useful diagnostic tools (intraductal ultrasonography and biopsy), endoscopic ultrasonography and associated fine needle aspiration (FNA) biopsy (14, 15). Diagnosis of lymph node metastasis by this examination is possible at this stage (15). At our institute, combinations of these imaging

modalities have been applied; however, the precise evaluation of cancer extension or node metastasis is still difficult before operation at this stage. In the next step, FNA or enhanced ultrasonography using a perflurobutane microbubble agent (Sonozoid[TM], GE Healthcare AS, Oslo, Norway) must be applied to determine the preoperative diagnosis (16). Preoperative diagnosis of node metastasis at the para-aortic region, which may be considered to be a contraindication of surgery, is still difficult by conventional modalities (17). Based on our experiences, positive predictive rate or sensitivity of diagnosis of para-aortic node metastasis are also low (data not published yet). Positron emission tomography or FNA may improve accuracy (18).

Although resectability of PC has been as improved described above, advanced carcinomas were still found at laparotomy, and 5 patients were inoperable at the time of laparotomy due to locally advanced tumor invading SMA, peritoneal carcinomatosis or tiny liver metastasis, despite the detailed preoperative image examinations in our series. At this stage, extended pancreatectomy might be predominantly performed in Japan because only surgical exploration in the surrounding tissues or nodes can accomplish high curability (2, 5, 6). In our series, most cases underwent PD including PPPD and DP with D2 lymphadenectomy. Complete lymphadenectomy at station number 162a and 16b1 are considered to be necessary because of a high rate of node metastasis (19). Combined resections of the portal vein or SMV were aggressively performed to accomplish R0 resection, as in other reports (5, 12, 20). Regarding combined resection of SMA, indication of radical operation is still controversial and, therefore, we did not

perform this operation. However, if the resected area was short and anastomosis is expected to be easy, combined resection of SMA or other major arteries would be considered in selected patients. Amano et al recently showed good results concerning this procedure (21). Morbidity after pancreatic resections in PC was not high in our series and we have not experienced mortality yet. In PC patients, the pancreas accompanied chronic pancreatitis and developed a hard architecture by fibrosis and, therefore, the prevalence of pancreatic fistula was lower than that in soft pancreas in other diseases (22).

With respect to stage of tumor, most PC patients except non-invasive IPMC showed advanced stages, which led to a poor prognosis in general. Furthermore, the dissected margin was positive at a relatively higher rate than the other cut-end margin. Other reports showed that R1 or R2 resection was not rare (23) in surgery of PC and cancer margin positivity might not always be related to longer survival (24). Waraya et al. (25) reported that the dissected peripancreatic margin was a powerful prognostic factor and, therefore, an 11% positive margin rate is an important problem to be solved in the next step. Postoperative adjuvant chemotherapy is a recent trend in patients with advanced PC beyond Stage III at our institute because the efficacy of adjuvant chemotherapy using gemcitabine or other combination chemotherapy has been clarified recently (10, 26, 27). The recurrence rate was also high and that in invasive ductal PC except IPNC was increased to 78% in our series, as well as in previous reports (28). We examined survival results and associated parameters in our series. The five year-survival in the present study was still low regardless of improvement of surgical techniques or perioperative

management, which was lower than that in previous reports (1-7, 29). As described above, the rate of dissected margin positive was not low and adjuvant chemotherapy has just been started recently. To improve the patients' prognoses, we attempted to perform more extensive surgery to resect surrounding tissues. Further long-term follow-up with adjuvant chemotherapy is necessary, using promising drugs such as S-1 or cisplatin combined with novel chemotherapies (26, 27). Hirata et al. stressed the significance of the Japanese stage of PC to reflect patient survival after surgery, and our present series showed similar results (20).

By clinical and histological examinations, serum CA19-9 level was a predictive marker for postoperative prognosis (25). In the present series, the median cut-off level of 85U/ml was applied and survival rates were increased according to increased level of CA19-9. To establish an adequate predictive value, receiver operating characteristics (ROC) analysis should be examined in a larger number of subjects in future studies. Changes of CA19-9 after surgery may be a useful follow-up marker (30). Cystic type or ductectatic type is a typical macroscopic finding of IPMN (31) and this type showed good outcomes as well as pathological diagnosis. Non-invasive IPMC is a proper indication for radical operation expecting long-term survival (32). However, invasive PC derived from IPMC showed a poor prognosis as well as invasive ductal carcinomas in our previous and present reports (33, 34). IPMC invading surrounding tissues or major vessels needs similar operations or adjuvant treatment to those in ordinary invasive PC. Various common predictive parameters in the digestive tract carcinomas were also associated

with poor outcomes in PC patients who underwent resection at our institute. Interestingly, invasions of the portal vein, SMV and splenic vein were not significantly associated with survival in these parameters. As described above, combined resection of these veins with pancreatic tissue was aggressively performed and the significance of this procedure was indicated as well as previous reports (2, 5, 12, 20). As described above, the dissected peripancreatic tissue margin and presence of residual tumor must be avoided to improve survivals and, therefore, extended pancreatectomy is still necessary.

In conclusion, aggressive surgical pancreatectomy was performed in 64 patients with pancreatic carcinomas including IPMC at a single cancer center over the past 15 years. Radical operation including combined resections of the portal system vein could be safely performed in many cases. Although results in only non-invasive IPMC were satisfactory, advanced invasive PC still showed a poor prognosis. Extended surgical resection to overcome R0 or cancer negative-margin is necessary as a curative treatment and, furthermore, newly effective adjuvant chemotherapy will be promising to improve patient survival in PC patients with poor prognostic factors.

REFERENCES

1. **Winter JM, Cameron JL, Campbell KA, Arnold MA, Chang DC, Coleman J, Hodgin MB, Sauter PK, Hruban RH, Riall TS, Schulick RD, Choti MA, Lillemoe KD, Yeo CJ:** 1423 pancreaticoduodenectomies for pancreatic cancer: A single-institution experience. J Gastrointest Surg. 2006;10:1199-1210.

2. **Kato K, Yamada S, Sugimoto H, Kanazumi N, Nomoto S, Takeda S, Kodera Y, Morita S, Nakao A:** Prognostic factors for survival after extended pancreatectomy for pancreatic head cancer: influence of resection margin status on survival. Pancreas. 2009;38:605-612.

3. **Kazanjian KK, Hines OJ, Duffy JP, Yoon DY, Cortina G, Reber HA:** Improved survival following pancreaticoduodenectomy to treat adenocarcinoma of the pancreas: the influence of operative blood loss. Arch Surg. 2008;143:1166-1171.

4. **Howard TJ, Krug JE, Yu J, Zyromski NJ, Schmidt CM, Jacobson LE, Madura JA, Wiebke EA, Lillemoe KD:** A margin-negative R0 resection accomplished with minimal postoperative complications is the surgeon's contribution to long-term survival in pancreatic cancer. J Gastrointest Surg. 2006;10:1338-1345

5. **Hirano S, Kondo S, Hara T, Ambo Y, Tanaka E, Shichinohe T, Suzuki O, Hazama K:** Distal pancreatectomy with en bloc celiac axis resection for locally advanced pancreatic body cancer: long-term results. Ann Surg. 2007;246:46-51.

6. **Kato K, Yamada S, Sugimoto H, Kanazumi N, Nomoto S, Takeda S, Kodera Y, Morita S, Nakao A:** Prognostic factors for survival after extended pancreatectomy

for pancreatic head cancer: influence of resection margin status on survival. Pancreas. 2009;38:605-612.

7. **Hellan M, Sun CL, Artinyan A, Mojica-Manosa P, Bhatia S, Ellenhorn JD, Kim J:** The impact of lymph node number on survival in patients with lymph node-negative pancreatic cancer. Pancreas. 2008;37:19-24.

8. **Yeo CJ, Cameron JL, Lillemoe KD, Sohn TA, Campbell KA, Sauter PK, Coleman J, Abrams RA, Hruban RH:** Pancreaticoduodenectomy with or without distal gastrectomy and extended retroperitoneal lymphadenectomy for periampullary adenocarcinoma, part 2: randomized controlled trial evaluating survival, morbidity, and mortality. Ann Surg. 2002;236:355-366

9. **Lockhart AC, Rothenberg ML, Berlin JD:** Treatment for pancreatic cancer: current therapy and continued progress. Gastroenterology. 2005;128:1642-1654.

10. **Sata N, Kurashina K, Nagai H, Nagakawa T, Ishikawa O, Ohta T, Oka M, Kinoshita H, Kimura W, Shimada H, Tanaka M, Nakao A, Hirata K, Yasuda H:** The effect of adjuvant and neoadjuvant chemo(radio)therapy on survival in 1,679 resected pancreatic carcinoma cases in Japan: report of the national survey in the 34th annual meeting of Japanese Society of Pancreatic Surgery. J Hepatobiliary Pancreat Surg. 2009;16:485-492.

11. **Japan Pancreas Society.** In: Kawarada Y ed. Classification of Pancreatic Carcinoma. 2nd Englsih ed., Tokyo: Kanehara & Co., Ltd., 2003, p.4-33

12. **Yekebas EF, Bogoevski D, Cataldegirmen G, Kunze C, Marx A, Vashist YK, Schurr PG, Liebl L, Thieltges S, Gawad KA, Schneider C, Izbicki JR:** En bloc vascular resection for locally advanced pancreatic malignancies infiltrating major blood vessels: perioperative outcome and long-term survival in 136 patients. Ann Surg. 2008;247:300-309.

13. **Pratt WB, Gangavati A, Agarwal K, Schreiber R, Lipsitz LA, Callery MP, Vollmer CM Jr:** Establishing standards of quality for elderly patients undergoing pancreatic resection. Arch Surg. 2009;144:950-956.

14. **Delbeke D, Pinson CW:** Pancreatic tumors: role of imaging in the diagnosis, staging, and treatment. J Hepatobiliary Pancreat Surg. 2004;11:4-10.

15. **Boujaoude J:** Role of endoscopic ultrasound in diagnosis and therapy of pancreatic adenocarcinoma. World J Gastroenterol. 2007;13:3662-3666.

16. **Sakamoto H, Kitano M, Komaki T, Imai H, Kamata K, Kimura M, Takeyama Y, Kudo M:** Small invasive ductal carcinoma of the pancreas distinct from branch duct intraductal papillary mucinous neoplasm. World J Gastroenterol. 2009;15:5489-5492

17. **Kala Z, Válek V, Hlavsa J, Hana K, Vánová A:** The role of CT and endoscopic ultrasound in pre-operative staging of pancreatic cancer. Eur J Radiol. 2007;62:166-169

18. **Sandha GS, Severin D, Postema E, McEwan A, Stewart K:** Is positron emission tomography useful in locoregional staging of esophageal cancer? Results of a

multidisciplinary initiative comparing CT, positron emission tomography, and EUS. Gastrointest Endosc. 2008;67:402-409.

19. **Shimada K, Sakamoto Y, Sano T, Kosuge T:** The role of paraaortic lymph node involvement on early recurrence and survival after macroscopic curative resection with extended lymphadenectomy for pancreatic carcinoma. J Am Coll Surg. 2006;203:345-352.

20. **Hirata K, Egawa S, Kimura Y, Nobuoka T, Oshima H, Katsuramaki T, Mizuguchi T, Furuhata T:** Current status of surgery for pancreatic cancer. Dig Surg. 2007;24:137-147.

21. **Amano H, Miura F, Toyota N, Wada K, Katoh K, Hayano K, Kadowaki S, Shibuya M, Maeno S, Eguchi T, Takada T, Asano T:** Is pancreatectomy with arterial reconstruction a safe and useful procedure for locally advanced pancreatic cancer? J Hepatobiliary Pancreat Surg. 2009;16:850-857.

22. **Yang YM, Tian XD, Zhuang Y, Wang WM, Wan YL, Huang YT:** Risk factors of pancreatic leakage after pancreaticoduodenectomy. World J Gastroenterol. 2005;11:2456-2461.

23. **Kato K, Yamada S, Sugimoto H, Kanazumi N, Nomoto S, Takeda S, Kodera Y, Morita S, Nakao A:** Prognostic factors for survival after extended pancreatectomy for pancreatic head cancer: influence of resection margin status on survival. Pancreas. 2009;38:605-612.

24. **Hernandez J, Mullinax J, Clark W, Toomey P, Villadolid D, Morton C, Ross S, Rosemurgy A:** Survival after pancreaticoduodenectomy is not improved by extending resections to achieve negative margins. Ann Surg. 2009;250:76-80.

25. **Waraya M, Yamashita K, Katagiri H, Ishii K, Takahashi Y, Furuta K, Watanabe M:** Preoperative serum CA19-9 and dissected peripancreatic tissue margin as determiners of long-term survival in pancreatic cancer. Ann Surg Oncol. 2009;16:1231-1240.

26. **Togawa A, Yoshitomi H, Ito H, Kimura F, Shimizu H, Ohtsuka M, Yoshidome H, Kato A, Sawada S, Miyazaki M:** Treatment with an oral fluoropyrimidine, S-1, plus cisplatin in patients who failed postoperative gemcitabine treatment for pancreatic cancer: a pilot study. Int J Clin Oncol. 2007;12:268-273.

27. **Murakami Y, Uemura K, Sudo T, Hayashidani Y, Hashimoto Y, Ohge H, Sueda T:** Impact of adjuvant gemcitabine plus S-1 chemotherapy after surgical resection for adenocarcinoma of the body or tail of the pancreas. J Gastrointest Surg. 2009;13:85-92.

28. **Nakao A, Fujii T, Sugimoto H, Kanazumi N, Nomoto S, Kodera Y, Inoue S, Takeda S:** Oncological problems in pancreatic cancer surgery. World J Gastroenterol. 2006;12:4466-4472.

29. **Kazanjian KK, Hines OJ, Duffy JP, Yoon DY, Cortina G, Reber HA:** Improved survival following pancreaticoduodenectomy to treat adenocarcinoma of the pancreas: the influence of operative blood loss. Arch Surg. 2008;143:1166-1171.

30. **Reni M, Cereda S, Balzano G, Passoni P, Rognone A, Fugazza C, Mazza E, Zerbi A, Di Carlo V, Villa E:** Carbohydrate antigen 19-9 change during chemotherapy for advanced pancreatic adenocarcinoma. Cancer. 2009;115:2630-2639.

31. **Ishida M, Egawa S, Aoki T, Sakata N, Mikami Y, Motoi F, Abe T, Fukuyama S, Sunamura M, Unno M, Moriya T, Horii A, Furukawa T:** Characteristic clinicopathological features of the types of intraductal papillary-mucinous neoplasms of the pancreas.Pancreas. 2007;35:348-352.

32. **Waters JA, Schmidt CM:** Intraductal papillary mucinous neoplasm--when to resect? Adv Surg. 2008;42:87-108.

33. **Woo SM, Ryu JK, Lee SH, Yoo JW, Park JK, Kim YT, Yoon YB:** Survival and prognosis of invasive intraductal papillary mucinous neoplasms of the pancreas: comparison with pancreatic ductal adenocarcinoma. Pancreas. 2008;36:50-55.

34. **Nanashima A, Sumida Y, Abo T, Oikawa M, Takeshita H, Hidaka S, Sawai T, Yasutake T, Kinoshita N, Hayashi T, Nagayasu T:** Surgical experiences of intraductal papillary mucinous neoplasms of the pancreas at a single Japanese institute: characteristics of malignant histology. Hepatogastroenterology. 2008;55:2238-2241.

Table 1. Comparison between overall 5-year survival after resection and clinical,

macroscopic parameters and postoperative chemotherapy

Parameters	5-year survival rates (%)	P value
CEA(ng/ml)		
≤10*	36	0.11
>10	20	
CA19-9 (U/ml)		
≤85*	46	0.048
>85	15	
Location of carcinoma		
Head	23	0.21
Body, Tail	43	
Macroscopic type#		
Cystic	86	
Ductectatic	100	0.01
Nodular	14	
Infiltrative	28	
Adjuvant chemotherapy		
No	33	0.84
Yes	29	

*; median value

#; findings according to *the Classification of Pancreatic Carcinoma* (11)

Table 2. Comparison between overall 5-year survival after resection and pathological

parameters

Parameters	5-year survival rates (%)	P value
T category#		
1	100	
2	33	0.03
3	14	
4	26	
Lymph node metastases#		
0	85	
1	6	0.01
2	0	
Station number 16a2 or 16b1	0	
Histological differentiation or type#		
Well differentiated adenocarcinoma	31	
Moderately	6	0.02
Poorly	23	
Non-invasive IPMC*	100	
Extrapancreatic nerve plexus invasion		
Absent	44	0.005
Present	12	
Serosal invasion#		
Absent	35	0.29
Present	14	
Retropancreatic tissue invasion#		
Absent	54	0.02
Present	6	
Distal bile duct invasion#		
Absent	46	0.002

Present	0	
Duodenal invasion#		
Absent	47	0.028
Present	0	
Portal venous system invasion#		
Absent	33	0.18
Present	16	
Arterial system invasion#		
Absent	31	0.012
Present	0	
Pancreatic cut-end margin#		
No	26	0.21
Cancer infiltration present	5	
Bile duct cut-end margin#		
No	28	0.01
Cancer infiltration present	0	
Dissected peripancreatic tissue margin#		
No	29	0.009
Cancer infiltration present	0	
Classification of lymph node dissection#		
D1	75	
D2	38	0.011
D3	15	
Residual tumor		
No	33	
Microscopic	5	0.11
Macroscopic	0	

*; intraductal papillary mucinous carcinoma

#; findings according to *the Classification of Pancreatic Carcinoma* (11)

Figure legend

Figure 1. Cumulative cancer-free (a) and overall (b) survival after hepatectomy.

Figure 2. Comparison between stages of tumor and cumulative cancer-free (a) and
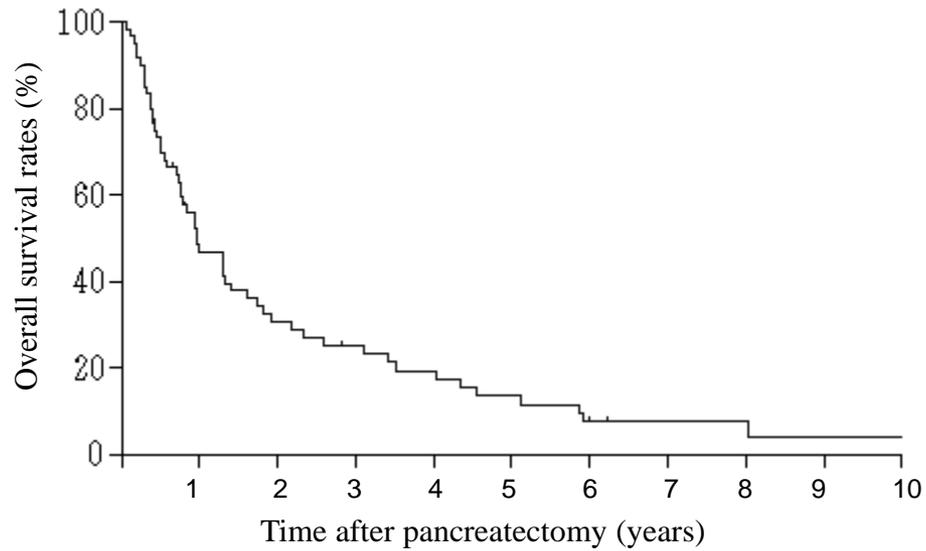
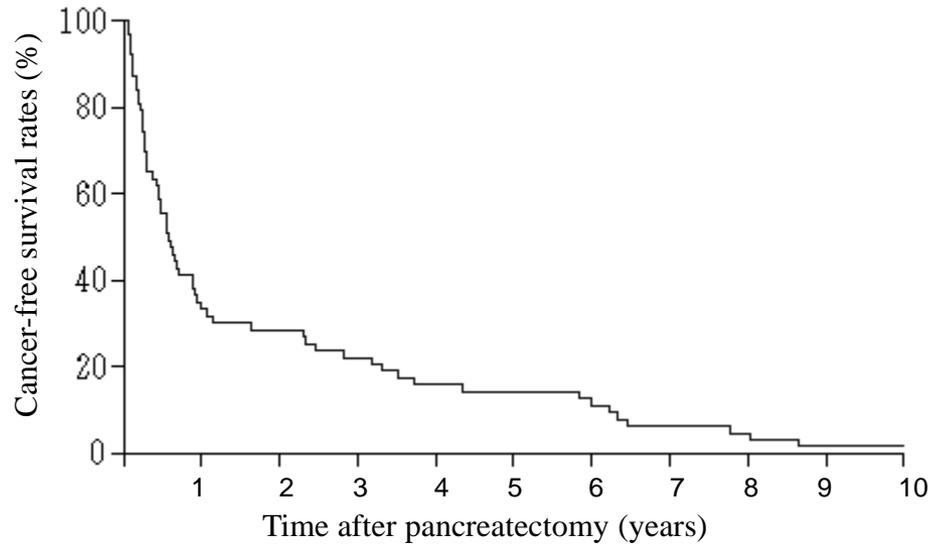overall (b) survival after hepatectomy.

Figure 1

Figure 2