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Survival outcome and prognostic factors of neoadjuvant treatment followed by resection for borderline resectable pancreatic cancer

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Purpose: Neoadjuvant treatment may provide improved survival outcomes for patients with borderline resectable pancreatic cancer (BRPC). The purpose of this study is to evaluate the clinical outcomes of neoadjuvant treatment and to identify prognostic factors.
Methods: Forty patients who met the National Comprehensive Cancer Network definition of BRPC and received neoadjuvant treatment followed by surgery between 2007 and 2015 were evaluated. Prospectively collected clinicopathological outcomes were analyzed retrospectively.
Results: The mean age was 61.7 years and the male-to-female ratio was 1.8:1. Twenty-six, 3, and 11 patients received gemcitabine-based chemotherapy, 5-fluorouracil, and FOLFIRINOX, respectively. The 2-year survival rate (2YSR) was 36.6% and the median overall survival (OS) was 20 months. Of the 40 patients, 34 patients underwent resection and the 2YSR was 41.2% while the 2YSR of patients who did not undergo resection was 16.7% (P = 0.011). The 2YSR was significantly higher in patients who had partial response compared to stable disease (60.6% *vs.* 24.3%, P = 0.038), in patients who did than did not show a CA 19-9 response after neoadjuvant treatment (40.5% *vs.* 0%, P = 0.039) and in patients who did than did not receive radiotherapy (50.8% *vs.* 25.3%, P = 0.036). Five patients had local recurrence and 17 patients had systemic recurrence with a median disease specific survival of 15 months.
Conclusion: Neoadjuvant treatment followed by resection is effective for BRPC. Pancreatectomy and neoadjuvant treatment response may affect survival. Effective systemic therapy is needed to improve long-term survival since systemic metastasis accounts for a high proportion of recurrence.
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Key Words: Pancreatic neoplasms, Neoadjuvant therapy, Surgery, Prognosis

INTRODUCTION

Pancreatic cancer is the fifth leading cause of cancer-related death in many developed countries and has a poor prognosis with a 5-year overall survival (OS) rate of approximately 7% [1,2]. Only 15%–20% of patients are diagnosed with early stages due to nonspecific symptoms and approximately 50% present with distant metastasis at the time of diagnosis. The remaining 30%–40% of patients have locally advanced disease with major vessel involvements [3].

Borderline resectable pancreatic cancer (BRPC) falls in the continuum between radiologically and technically resectable and unresectable cancer [3]. The National Comprehensive Cancer Network (NCCN) guidelines define borderline resectable

as involvement of veins including superior mesenteric vein (SMV) or portal vein (PV), involvement of arteries including the gastroduodenal artery, hepatic artery, superior mesenteric artery (SMA) or celiac axis [4]. However, the definition of BRPC differs between institutions and some of these criteria are highly subjective leading to varying treatment outcomes depending on the definition used.

In a previous study, 35 patients with BRPC treated with radiation and either 5-fluouracil (5-FU)/cisplatin or gemcitabine-based chemotherapy resulted in a surgical resection rate of 79% and a median OS of 24.5 months compared with a median OS of 18.5 months in patients who received surgery alone [5]. Furthermore, in a retrospective review of 160 patients divided into 3 groups based on the disease status or performance/medical status, reported resection rates following neoadjuvant treatment of 38%, 50%, and 38%, respectively. Within each group, the median OS was longer in patients who did than did not undergo resection [3]. Moreover, in a recent meta-analysis, the resection rate of BRPC patients treated with concurrent chemoradiotherapy (CCRT) prior to surgery was 80.4% (95% confidence interval [CI], 66.2–89.6), median OS 12.4 months (range, 9–16 months), and 1- and 2-year survival rates (YSRs) were 61% and 44% [6]. However, the definitions of unresectable or borderline resectable are inconsistent among different studies. Therefore, this study aims to assess clinical outcomes of neoadjuvant treatment followed by surgery in patients with BRPC and to identify factors associated with a favorable prognosis.

METHODS

Patient selection

Between 2007 and 2015, 2,056 patients at the Seoul National University Hospital (SNUH) were radiologically diagnosed with pancreatic cancer. A total of 187 patients met the NCCN criteria for BPRC: an absence of distal metastases; CT findings of venous distortion of the SMV/PV axis including short-segment venous occlusion with sufficient proximal and distal vessel length allowing safe reconstruction; encasement of the gastroduodenal artery up to the hepatic artery with either short-segment encasement or direct abutment of the hepatic artery without extension to the celiac axis; and tumor abutment of the SMA involving ≤180° of the vessel wall circumference [4].

Resectability was assessed by quadruple-phase pancreatobiliary protocol CT imaging consisting of precontrast, early arterial, pancreatic, and venous phases [7]. Of the 187 patients who met the NCCN criteria for BPRC, 67 patients underwent surgery without neoadjuvant treatment while 62 patients received chemotherapy and/or radiotherapy alone and 18 patients were untreated. The remaining 40 patients received neoadjuvant treatment followed by surgery. Pancreatic head cancer

along with body or tail cancer patients were included in these 40 patients.

This retrospective study conformed to the ethical guidelines of the Declaration of Helsinki and was approved by the Institutional Review Board of the SNUH (approval number: 1308-107-516). Written informed consent was waived by IRB.

Neoadjuvant chemotherapy/radiotherapy

The choice of chemotherapy and/or radiotherapy was determined by each patient's general performance and ease of access to the hospital. Neoadjuvant chemotherapy regimens included gemcitabine, conventional 5-FU, or FOLFIRINOX. Gemcitabine chemotherapy consisted of 400 mg/m^2 body surface area (BSA) intravenous gemcitabine administered weekly for 6 weeks. Three-dimensional conformal radiotherapy consisted of a total dose of 45 Gy (1.8 Gy daily fraction, 5 fractions per week for 5 weeks) with a boost dose of 9 Gy (1.8 Gy daily fraction, 5 fractions). 5-FU based CCRT consisted of 20-Gy dose to the tumor given in 10 daily fractions over a 2-week period plus an intravenous bolus of 5-FU (500 mg/m^2 of BSA on each of the first 3 days of radiotherapy and again after a planned break of 2 weeks). FOLFIRINOX consisted of oxaliplatin at a dose of 85 mg/m^2 followed by leucovorin at a dose of 400 mg/m^2 both administered as a 2-hour intravenous infusion with the addition of 180 mg/m^2 irinotecan after 30 minutes given over 90 minutes as an intravenous infusion. This treatment was followed by 5-FU at a dose of 400 mg/m^2 administered as an intravenous bolus followed by a continuous infusion of 2,400 mg/m^2 for a 46-hour period (one cycle) every 2 weeks.

Doses were reduced depending on the patient's status or when adverse events were noted. Treatment related toxicities were evaluated by the National Cancer Institute Common Terminology Criteria of Adverse Events (NCI-CTCAE) [8].

Tumor response assessment

Tumor responses after neoadjuvant treatment were assessed radiologically with pancreatobiliary protocol CT or MR and were categorized as complete remission (CR), partial remission (PR), stable disease (SD), or progressive disease (PD) according to the new response evaluation criteria in solid tumors suggested in the revised Response Evaluation Criteria In Solid Tumors (RECIST) guidelines [9]. Serum concentrations of CA 19-9 were measured at the first visit to the hospital, after neoadjuvant treatment and after surgery.

Operation

Patients were evaluated for surgical eligibility after neoadjuvant chemotherapy. When resection was to proceed, surgery was performed 4–8 weeks from the end date of neoadjuvant treatment. Operation type was decided depending on the tumor location. Pylorus preservation was attempted in all pa-

tients undergoing pancreaticoduodenectomy with the exception of coexistence of duodenal ischemia, ulcer, or tumor infiltration. Lymph node dissection in patients undergoing pancreaticoduodenectomy included removal of regional lymph nodes to the right side of the celiac artery and SMA and all soft tissues in the hepatoduodenal ligament except for the PV and hepatic artery [10]. Distal pancreatectomy was performed with the standard procedure. The pancreatic parenchyma was divided using electrocautery and blade. The main pancreatic duct was ligated with nonabsorbable sutures and the transected pancreas was occluded with interlocking interrupted mattress sutures of 4-0 black silk and reinforced with 4-0 polypropylene (Prolene; Ethicon Inc., Somerville, NJ, USA) [11].

Adjuvant chemotherapy and/or radiotherapy

Adjuvant chemotherapy and/or radiotherapy was recommended to patients after operation. Similar to neoadjuvant treatment, the regimen was determined considering each patient's general performance and ease of access to the hospital along with consideration of the previous treatment regimen. Adjuvant treatment regimen included gemcitabine, conventional 5-FU, or FOLFIRINOX.

Statistical analysis

Continuous data were expressed as means ± standard deviations. Categorical variables were compared using the Pearson chi-square test, and continuous variables using Student t test. All parameters with a P-value of <0.05 by univariate analysis were included in the multivariate model. Survival and recurrence information were reviewed. Disease-specific survival was calculated using the Kaplan-Meier method and compared by the log-rank test. All statistical analyses were performed using IBM SPSS Statistics ver. 21.0 (IBM Co., Armonk, NY, USA).

RESULTS

Demographic findings

Patient demographics and clinical characteristics are summarized in Table 1. The 40 patients consisted of 26 men and 14 women with a mean age of 61.7 years and median follow-up period of 16 months (range, 7–46 months). Of the 40 patients, 22 patients met the artery criteria for BRPC and 18 patients with the vein criteria. Gemcitabine-based chemotherapy, 5-FU-based chemotherapy and FOLFIRINOX were administered in 26, 3, and 11 patients respectively. In addition, 25 patients received radiotherapy. Surgically, 12 patients underwent pylorus-preserving pancreaticoduodenectomy while 11 underwent Whipple's operation. Eight patients underwent distal pancreatectomy while 3 patients received total pancreatectomy. Six patients underwent open biopsy or bypass surgery due to advanced stages including evidence of distant metastasis. A

Table 1. Patient characteristics (n = 40)

Characteristic	Value
Age (yr), mean ± SD	61.7 ± 8.4
Sex, male:female	26:14
Tumor location	
Head	28 (70.0)
Body/tail	11 (27.5)
Diffuse	1 (2.5)
Vessel involvement	
Artery	22 (55.0)
Vein	18 (45.0)
Neoadjuvant treatment	
Chemotherapy with radiotherapy	25 (62.5)
Chemotherapy without radiotherapy	15 (37.5)
Neoadjuvant chemotherapy regimen	
Gemcitabine	26 (65.0)
5-FU	3 (7.5)
FOLFIRINOX	11 (27.5)
Operation	
PPPD	12 (30.0)
Whipple's operation	11 (27.5)
Distal pancreatectomy	8 (20.0)
Total pancreatectomy	3 (7.5)
Open biopsy, bypass surgery	6 (15.0)
Combined vessel resection	9 (22.5)
Follow-up (mo), median (range)	16 (7–46)

Values are presented as number (%) unless otherwise indicated.
SD, standard deviation; 5-FU, 5-fluorouracil; PPPD, pylorus preserving pancreaticoduodenectomy.

total of nine patients underwent combined vessel resection and reconstruction.

Responses to neoadjuvant treatment

Tumor response to neoadjuvant treatment is summarized in Table 2. The mean tumor diameter decreased from 3.2 cm to 2.5 cm with a mean reduction of 23.2%. Only 4 patients showed no change or rather an increase in size (range, 0%–13%) with the remaining 36 patients with size decreases as high as from 3.8 to 1.3 cm, a reduction of 65.7%. According to the RECIST criteria, 14 patients achieved PR and 26 showed SD. None of the patients showed CR or PD. The response was not associated with the chemotherapy regimen the patient received (P = 0.692).

The mean serum CA 19-9 level decreased from 1,150.5 ± 2,344.5 U/mL prior to surgery to 449.2 ± 1,907.4 U/mL after neoadjuvant treatment. Of the 40 patients, 34 patients showed a decrease in CA19-9 concentration after neoadjuvant treatment whereas 6 showed no change or increased levels.

Morbidities of neoadjuvant treatment and surgery

Toxicities and morbidities of neoadjuvant treatment were evaluated based on the NCI-CTCAE (Table 3). The most common all grade toxicity was nausea (47.5%) followed by neutropenia

Table 2. Neoadjuvant treatment response

Variable	Value
Tumor size (mm)	
Preneoadjuvant treatment	3.2 ± 0.9
Postneoadjuvant treatment	2.5 ± 1.0
Size change (%)	−23.2 ± 18.6
RECIST criteria	
Complete remission	0 (0)
Partial remission (PR)	26 (65.0)
Stable disease	14 (35.0)
Progressive disease	0 (0)
PR according to the regimen	P = 0.692
Gemcitabine (n = 26)	8 (30.8)
5-FU (n = 3)	1 (33.3)
FOLFIRINOX (n = 11)	5 (45.4)
CA19-9 (U/mL)	
Preneoadjuvant treatment	1,150.5 ± 2,344.5
Postneoadjuvant treatment	449.2 ± 1,907.4

Values are presented as mean ± standard deviation or number (%). SD, standard deviation; 5-FU, 5-fluorouracil; PR, partial remission.

Table 3. Morbidity of neoadjuvant treatment and surgery

	Grade 3–4	All grade
Neoadjuvant treatment toxicities		
Neutropenia	-	19 (47.5)
Thrombocytopenia	-	15 (37.5)
Anemia	-	8 (20.0)
Neutropenic fever	2 (5)	3 (7.5)
Fatigue	-	4 (10.0)
Anorexia	-	7 (17.5)
Abdominal pain	1 (2.5)	13 (32.5)
Epigastric pain	1 (2.5)	5 (12.5)
Nausea	3 (7.5)	20 (50.0)
Vomiting	3 (7.5)	12 (30.0)
Diarrhea	-	5 (12.5)
Constipation	-	6 (15.0)
LFT elevation	-	2 (5.0)
Cholangitis	2 (5)	3 (7.5)
Surgical morbidities		
Bovine patch thrombus	-	1 (2.9)
Delayed gastric emptying	-	1 (2.9)
Hepaticojejunostomy leakage	-	1 (2.9)
Ascites	-	1 (2.9)
CDAD	-	1 (2.9)
Chyle leakage	-	1 (2.9)
Postoperative ileus	-	2 (5.8)
Wound problem	-	3 (8.8)
POPF		
Grade A	-	7 (20.6)
Grades B, C	-	0 (0)

Values are presented as number (%).
LFT, liver function test; CDAD, *Clostridium difficile* associated diarrhea; POPF, postoperative pancreatic fistula.

and thrombocytopenia. The most common grade 3/4 toxicities were nausea (7.5%) and vomiting (7.5%).

Of the 34 patients who underwent surgical resection, 17 patients experienced postoperative morbidities (50.0%). The most frequent being grade A postoperative pancreatic fistula (POPF, 20.6%) followed by wound complications (8.8%) and ileus (5.8%). One patient experienced both POPF and ileus. Other morbidities are summarized in Table 3. There was no in-hospital death associated with surgical complications.

Pathologic findings
Pathologic findings are summarized in Table 4. Of the 34

Table 4. Pathologic findings

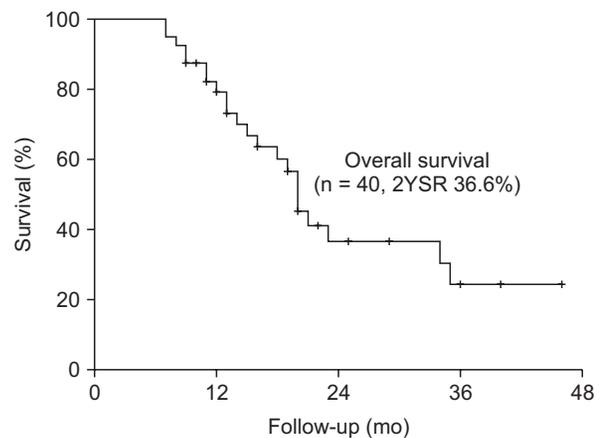| Variable	Number (%)
Resection rate	34 (85.0)
Resection margin	
R0	26 (76.4)
R1	4 (11.8)
R2	4 (11.8)
T stage	
T0	1 (2.9)
T1	4 (11.7)
T2	2 (5.9)
T3	24 (70.6)
T4	3 (8.9)
Lymph node metastasis	8 (23.5)
Lymphatic invasion	9 (26.5)
Venous invasion	12 (35.3)
Perineural invasion	24 (70.6)
Tumor regression grade	
Grade 0	1 (2.9)
Grade 1	12 (35.3)
Grade 2	14 (41.2)
Grade 3	5 (14.7)
Not evaluated	2 (5.9)

Fig. 1. Overall survival curve after neoadjuvant treatment followed by operation. 2YSR, 2-year survival rate.

patients who underwent surgical resection, R0 resection was performed in 26 patients while R1 resection was performed in 4 cases. Furthermore, R2 resection was performed in 4 patients. Of these 34 patients, eight patients were positive for lymph node invasion (23.5%) while 9 patients were present with angiolymphatic invasion (26.5%). Also, venous invasion was observed in 12 cases (35.3%) while perineural invasion was observed in 24 patients (70.5%).

Adjuvant treatment

Of the 34 patients who received surgical resection, gemcitabine-based, 5-FU-based and FOLFIRINOX chemotherapy regi-
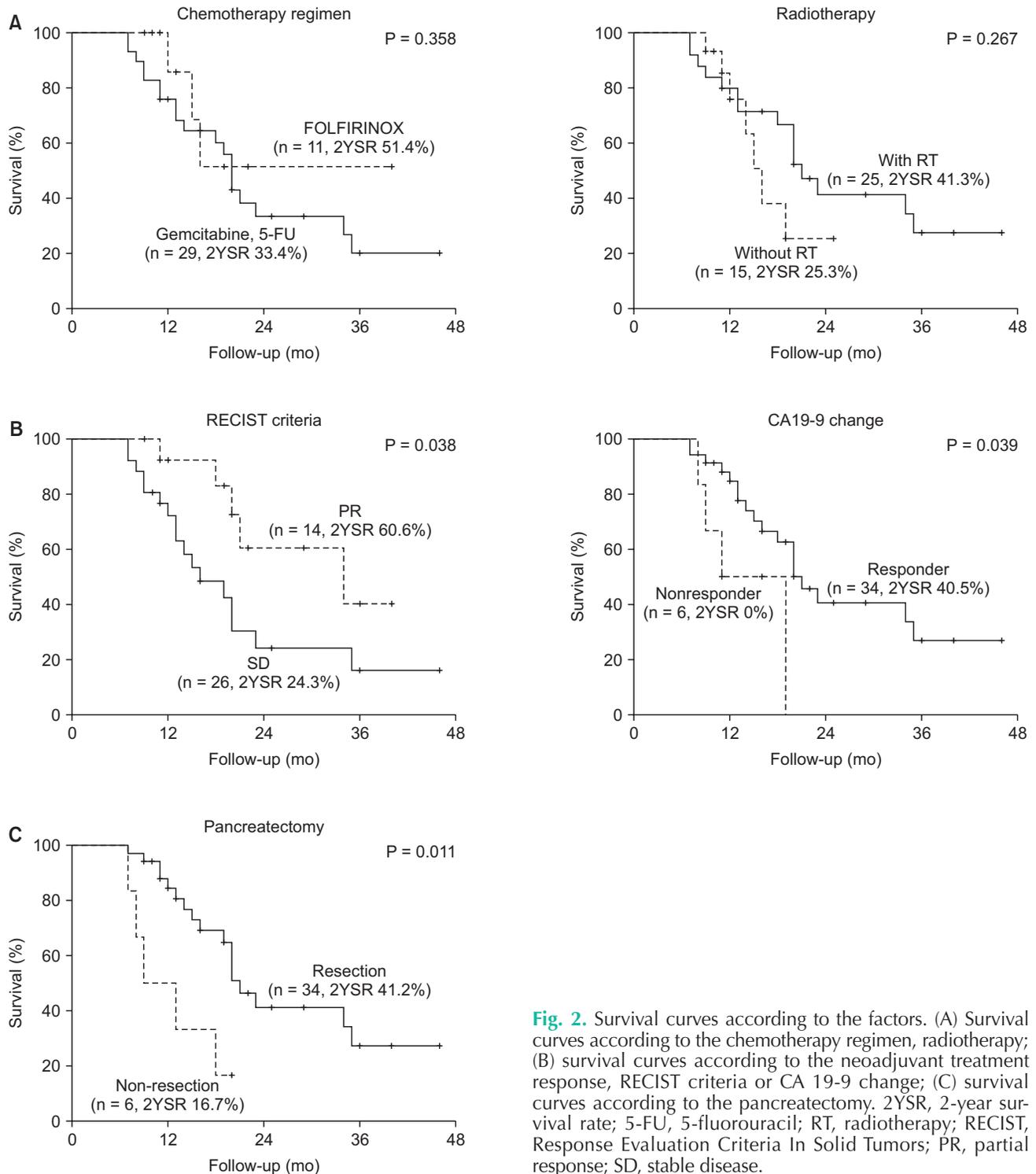

Fig. 2. Survival curves according to the factors. (A) Survival curves according to the chemotherapy regimen, radiotherapy; (B) survival curves according to the neoadjuvant treatment response, RECIST criteria or CA 19-9 change; (C) survival curves according to the pancreatectomy. 2YSR, 2-year survival rate; 5-FU, 5-fluorouracil; RT, radiotherapy; RECIST, Response Evaluation Criteria In Solid Tumors; PR, partial response; SD, stable disease.

men were given to 17, 11, and 3 patients respectively. The remaining 2 patients presented with recurrence before receiving adjuvant treatment and 1 patient did not receive further therapy because of poor performance status. On the other hand, out of the 6 patients who received open biopsy or bypass surgery, 4 patients received gemcitabine-based chemotherapy whereas 2 patients did not receive any further treatment.

Survival outcomes

The median OS was 20 months and the 1-, 2-, and 3-YSRs were 79.3%, 36.6%, and 24.2% respectively (Fig. 1). The 2YSRs was similar in patients who received gemcitabine/5-FU and FOLFIRINOX (33.4% *vs.* 51.4%, P = 0.358) and in patients who did and did not receive radiotherapy (41.3% *vs.* 25.3%, P = 0.267) (Fig. 2A). In contrast, the 2YSRs were significantly higher in patients who achieved PR than SD in the neoadjuvant setting (60.6% *vs.* 24.3%, P = 0.038) and in patients showed a reduction in CA 19-9 concentration after neoadjuvant treatment compared

Table 5. Prognostic factors (univariate analysis)

Variable	Number	2YSR (%)	P-value
Chemotherapy regimen, Gem+5-FU/FOLFIRINOX	29/11	33.4/51.4	0.358
Radiotherapy, yes/no	25/15	41.3/25.3	0.267
RECIST criteria, PR/SD	14/26	60.6/24.3	0.038
CA19-9 change, yes/no	34/6	40.5/0	0.039
Pancreatectomy, yes/no	34/6	41.2/16.7	0.011
N stage, N0/N+	26/8	42.6/34.3	0.477
Lymphatic invasion, -/+	25/9	36.1/50.0	0.297
Venous invasion, -/+	22/12	39.0/44.4	0.941
Perineural invasion, -/+	10/24	64.3/33.4	0.182
Adjuvant regimen, Gem/5-FU/FOLFIRINOX	17/11/13	22.1/42.4/100.0	0.282

2YSR, 2-year survival rate; Gem, gemcitabine; 5-FU, 5-fluorouracil; RECIST, Response Evaluation Criteria In Solid Tumors; PR, partial response; SD, stable disease.
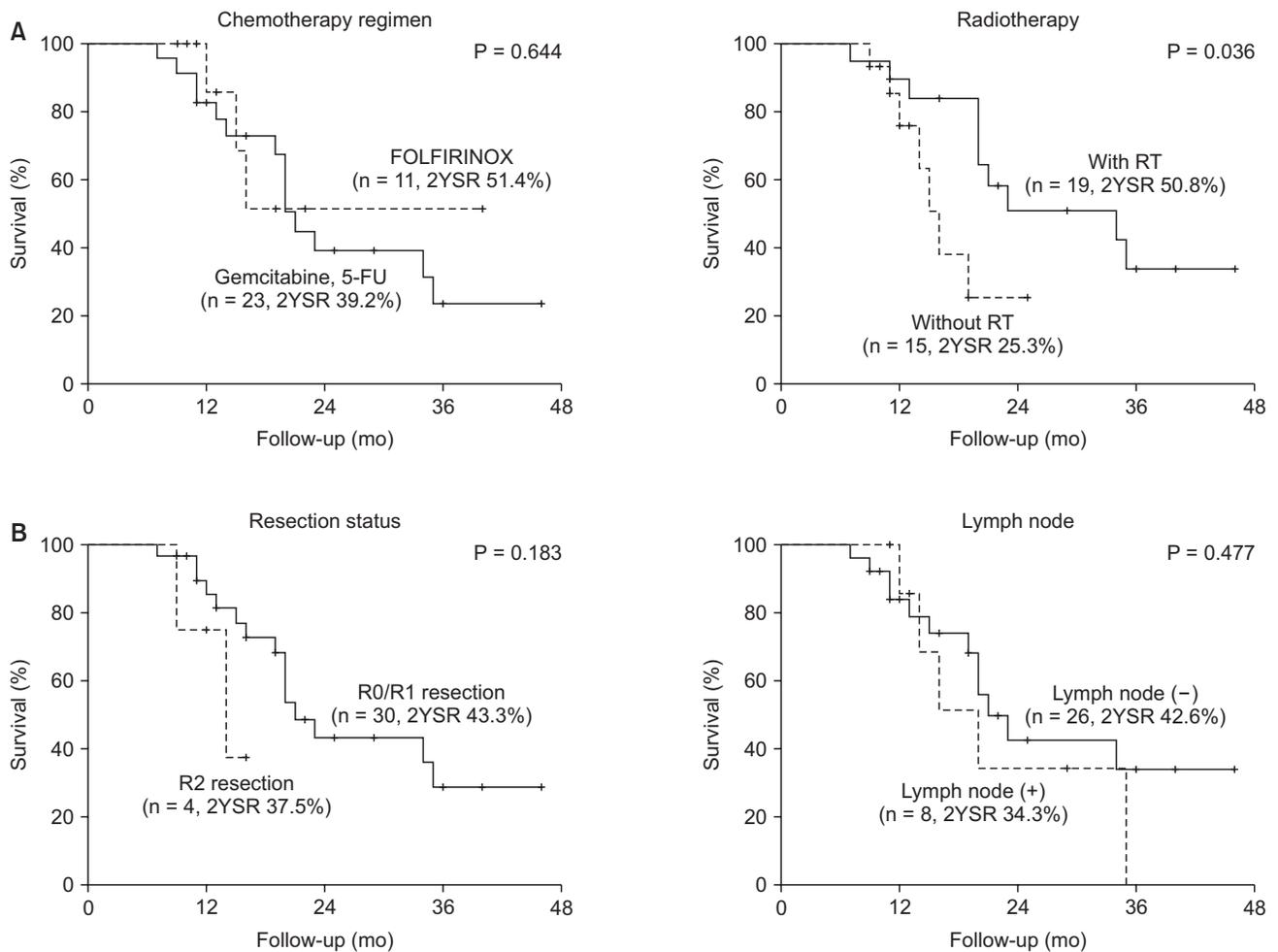

Fig. 3. Pancreatectomy subgroup survival curves according to the factors. (A) Survival curves according to the chemotherapy regimen, radiotherapy; (B) survival curve according to the resection status, lymph node metastasis. 2YSR, 2-year survival rate; 5-FU, 5-fluorouracil; RT, radiotherapy.

to those who did not (40.5% *vs.* 0%, P = 0.039) (Fig. 2B). Patients who underwent pancreatectomy also showed significantly higher 2-year OS than patients who underwent open biopsy or bypass surgery (41.2% *vs.* 16.7%, P = 0.011) (Table 5, Fig. 2C).

Prognostic factors for survival

In univariate analyses, PR, reduced CA 19-9 level and pancreatectomy were associated with a better outcome (Table 5). In multivariate analyses, PR (odds ratio [OR], 0.264; 95% CI, 0.091–0.772; P = 0.015) and pancreatectomy (OR, 0.181; 95% CI, 0.058–0.561; P = 0.003) were independent variables affecting outcomes.

After a subgroup analysis of 34 patients who underwent resection, the 2YSR was significantly high in patients who received RT than those who did not (50.8% *vs.* 25.3%, P = 0.036). However, survival was not associated with resection status, vessel involvement, neoadjuvant chemotherapy regimen, CA 19-9 response, combined vessel resection, lymphatic invasion, venous invasion, perineural invasion and adjuvant treatment regimen (Table 5, Fig. 3).

Recurrence

Of the 34 patients who underwent surgical resection, 22 patients developed tumor recurrence (58%) with a median disease free survival of 15 months (range, 2–40 months) (Fig. 4). Of these 22 patients, 5 patients showed locoregional recurrence while 17 patients had systemic recurrence. Two patients presented with recurrence before commencing adjuvant treatment.

Recurrence was significantly associated with the neoadjuvant chemotherapy regimen favoring FOLFIRNOX (P = 0.046). In contrast, recurrence was unassociated with radiotherapy, neoadjuvant treatment response, resection status and T or N stage.
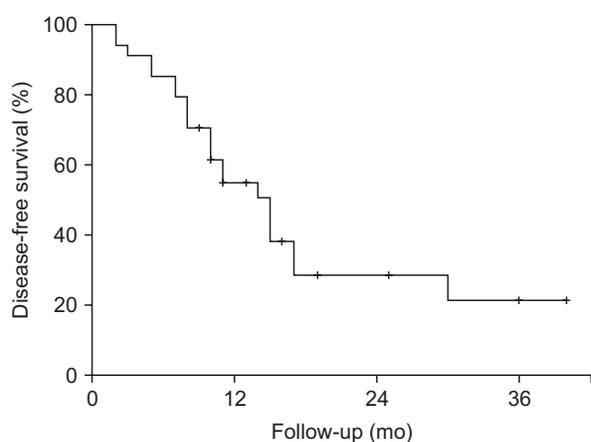

Fig. 4. Disease-free survival curve after neoadjuvant treatment followed by operation.

DISCUSSION

BRPC is a locally advanced disease with involvement of the surrounding major vessels and is present in 30%–40% of patients with pancreatic cancer at diagnosis [3]. The definition of BRPC has been found to vary among studies. Thus, the difference between resectable and unresectable disease is unclear and confusing. The NCCN and the MD Anderson Cancer Center proposed definition of BRPC is the widely accepted, but there is no universally accepted definition to present date [12]. Because the definition of BRPC can include varying degrees of involvement of the major vessels, a more conventional definition is required to compare study results and select appropriate treatment.

Neoadjuvant treatment including chemotherapy and/or radiotherapy is beneficial for node-negative patients undergoing microscopic curative resection. Neoadjuvant treatment has shown survival benefits compared to surgery alone, not only in patients with resectable pancreatic cancer but also in those with locally advanced tumors [13-17]. BRPC patients who received neoadjuvant treatment had a median OS of 20 months and a 2YSR of 36.6%. In contrast, the 67 patients who underwent surgery without neoadjuvant treatment had a median OS of 16 months and a 2YSR of 28.9% whereas 62 patients who received chemotherapy and/or radiotherapy without surgery had a median OS of 12 months and a 2YSR of 9.8%. The 18 untreated patients had a median OS of 7 months and a 2YSR of 0%. The four groups showed statistically significant (P < 0.001; detailed data not shown). These findings along with other studies conducted indicate that neoadjuvant treatment followed by surgery is more effective than first-line surgery in the BRPC.

Adjuvant chemotherapy regimens widely used in pancreatic cancer patients include gemcitabine and 5-FU [18,19]. FOLIRINOX was recently introduced as a treatment of metastatic pancreatic cancer as this regimen showed better median OS than gemcitabine-based treatment (11 months *vs.* 6.8 months) [20]. Good performance status is required because FOLFIRINOX has serious adverse effects [21]. FOLFIRINOX is a new neoadjuvant treatment option [22]. In this study, the recurrence rate was significantly low in patients treated with FOLFIRINOX compared to patients treated with gemcitabine or conventional 5-FU regimens. Moreover, median OS was longer and neoadjuvant treatment response was better in FOLFIRINOX treated patients although, these differences were not statistically significant. Further investigations are needed to determine whether FOLFIRINOX should be considered a standard neoadjuvant treatment regimen in patients with BRPC.

The benefit of neoadjuvant radiotherapy is less clear. In our study, 25 patients out of 40 patients received concurrent chemotherapy and radiotherapy. Radiotherapy was not associated with better survival or recurrence. However, subgroup analysis

revealed that patients undergoing pancreatectomy showed significantly higher 2-year OS rate than those who did than did not receive radiotherapy (50.8% *vs.* 25.3%, P = 0.036). A study of patients with localized unresectable pancreatic cancer found that median OS was significantly longer in patients receiving radiotherapy plus gemcitabine than patients receiving gemcitabine alone (11.1 months *vs.* 9.2 months, P = 0.017) [23]. In addition, another study reported that there is no difference in survival between patients receiving 5-FU based chemotherapy plus radiotherapy and those receiving 5-FU alone, although the toxicity rate was higher in the former group [24].

The 2YSR was significantly higher in patients who underwent pancreatectomy after neoadjuvant treatment than in patients who underwent open biopsy or bypass surgery (41.2% *vs.* 16.7%, P = 0.011). Of the 34 patients who underwent pancreatectomy, R0 resection was achieved in 26 patients (76.4%). The 2YSRs of R0, R1, and R2 resections were 44.7%, 66.7%, and 37.5% respectively. The high survival rate of R1 resection is thought to be an effect of small sample sized. Thus, pancreatectomy itself is an important prognostic factor for survival and R0 resection rate increased after neoadjuvant treatment which is consistent with the results of other studies [6].

However, 22 out of the 34 patients who underwent pancreatectomy experienced recurrence including 17 patients who experienced systemic recurrence. Despite pancreatectomy and increased R0 resection rate after neoadjuvant treatment, the high incidence of systemic recurrence had a deleterious effect on survival outcomes suggesting the need for an effective maintenance therapy.

This study has several limitations. First, due to the retrospective nature of this study, neoadjuvant chemotherapy regimen varied among patients. Second, the small number of study subjects made meaningful analysis difficult and prevented firm conclusions. Third, the follow-up period was insufficient. Prospective studies assessing single or fixed neoadjuvant treatment regimens in larger number of patients with longer follow-up period is needed.

In conclusion, neoadjuvant treatment followed by resection is an effective approach for BRPC. The most important prognostic factor affecting survival after neoadjuvant treatment was resection itself. The RECIST criteria and reduced serum CA 19-9 concentration were associated with biologic response. Radiotherapy may also affect survival after neoadjuvant treatment followed by resection. Most recurrences were observed in systemic metastasis. Thus, the development of effective systemic therapy as well as R0 resection is needed to prolong long-term survival.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGEMENTS

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