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Improved Survival in Patients with Resected Pancreatic Carcinoma Using Postoperative Intensity-Modulated Radiotherapy and Regional Intra-Arterial Infusion Chemotherapy

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Background: We assessed the role of adjuvant intensity-modulated radiotherapy (IMRT) in combination with chemotherapy for pancreatic carcinomas after curative resection and identified prognostic factors related to pancreatic carcinoma after multidisciplinary treatment strategies.

Material/Methods: Pancreatic carcinoma patients (n=61) who received adjuvant radiotherapy after resection (median dose, 50.4 Gy) between 2010 and 2016 were retrospectively identified. Sixty patients received chemotherapy, including concurrent chemoradiotherapy (CCRT), systemic chemotherapy, and regional intra-arterial infusion chemotherapy (RIAC). The Kaplan-Meier method was used to measure the 3-year overall survival (OS) and disease-free survival (DFS) rates. Log-rank univariate analysis and multivariate Cox regression model analysis were used to identify prognostic factors.

Results: Median follow-up time was 25.5 (range, 4.9–59.7) months. The 3-year OS and DFS rates were 31.0% and 16.1%, respectively. The median OS and DFS were 27.4 and 16.7 months, respectively. Multivariate analysis indicated that independent favorable predictors for OS were CCRT (p=0.039) and postoperative RIAC (p=0.044). Moreover, postoperative RIAC (p=0.027), and pre-radiotherapy CA19-9 ≤37 U/mL (p=0.0080) were independent favorable predictors for DFS. The combination of radiotherapy and chemotherapy was tolerated well by the patients, and no treatment-related death occurred.

Conclusions: Combined IMRT and adjuvant chemotherapy appeared safe and effective for pancreatic carcinoma. CCRT was associated with improved survival with acceptable toxicity. We propose that radiotherapy could be a part of postoperative treatment, but it should be administered concurrently with chemotherapy. Adding RIAC was associated with improved OS and DFS and it could be integrated into the postoperative treatment regimen.

MeSH Keywords: Chemotherapy, Cancer, Regional Perfusion • Pancreatectomy • Pancreatic Neoplasms • Radiotherapy • Survival

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Background

The incidence of pancreatic carcinoma has increased dramatically over the past few decades. In 2012, its estimated incidence and mortality ranked 10th and 6th, respectively, among cancers worldwide [1]. Surgery is the sole curative modality for pancreatic carcinoma; however, only 20% of patients are candidates for curative resection when the disease is diagnosed [2]. Moreover, the prognosis of pancreatic carcinoma after surgery remains dismal, with a median survival time of 14–20 months [3]. Despite efforts to improve survival with multidisciplinary approaches, the prognosis remains poor.

Currently, adjuvant chemotherapy is the standard treatment after curative surgery of pancreatic carcinoma, and it is more beneficial in improving outcomes compared with surgery alone [4,5]. A meta-analysis has indicated a clear trend toward increased survival using concurrent chemoradiotherapy (CCRT) compared to radiotherapy (RT) alone for locally advanced pancreatic carcinoma [6]. However, whether adjuvant therapy consisting of CCRT can further improve outcome of resected pancreatic carcinoma is controversial [7–11]. Historically, a phase II randomized (EORTC-40013-22012) study showed that CCRT offered greater local control benefit than chemotherapy alone [7]. Furthermore, 2 American studies also demonstrated the therapeutic benefits of adjuvant CCRT [10,11]. In contrast, a large, multicenter trial (ESPAC 1) showed that radiotherapy might be detrimental to outcomes after resection for pancreatic cancer [8,9]. Therefore, the studies published to date have not been able to confirm the role of radiotherapy as adjuvant therapy after surgery. Moreover, it is believed that the irradiation technology used in some previous studies was outdated, and included, for example, split-course radiotherapy or an inappropriate total irradiation dose.

As a particular method of chemotherapy, regional intra-arterial chemotherapy (RIAC) is also an option for the management of pancreatic carcinoma, but its efficacy has not been confirmed. Theoretically, RIAC could improve locoregional control and prevent liver metastasis for patients with pancreatic carcinoma by delivering high concentrations of chemotherapeutic agents to the tumor bed and liver, but it did not increase the toxicities when compared to systemic chemotherapy [12]. However, there is no consensus on the benefit of this therapy [12–14].

Hence, we conducted the present study to assess the efficacy of postoperative prophylactic radiotherapy to the tumor bed and elective nodes using postoperative intensity-modulated radiation therapy (IMRT) combined with adjuvant chemotherapy, including systemic chemotherapy and RIAC for pancreatic carcinomas.

Material and Methods

Patient selection

A retrospective medical information review was performed on all patients with resected pancreatic carcinoma who underwent postoperative adjuvant radiotherapy at Fudan University Shanghai Cancer Center between March 2010 and January 2016. Patients included were those who: (1) had histologically confirmed pancreatic carcinoma, (2) had undergone potentially curative resection, and (3) had received postoperative radiotherapy alone or in combination with chemotherapy. The exclusion criteria were: (1) the presence of neuroendocrine tumors, (2) occurrence of local or distant failure prior to RT, and (3) follow-up record uncompleted. Finally, 61 patients with stage T1-3N0-1M0 matched the selection criteria and were enrolled in our analysis. The characteristics of patients and treatment details are listed in Table 1.

Treatment regimens

Among the 61 patients, 32 (52.5%) patients underwent pancreaticoduodenectomy, 27 (44.3%) underwent distal pancreatectomy, and 2 (3.3%), underwent total pancreatectomy. After surgical resection, adjuvant radiotherapy was administered as IMRT with a 6-MeV x-ray. A CT simulation was acquired to determine the target volumes. The clinical target volume (CTV) encompassed the surgical bed and elective nodal regions, which included the hepatic, celiac, and superior mesenteric vessels with expansions of 1–2 cm. Extra margins of 0.5–1.0 cm were added around the CTV to obtain the planning target volume (PTV), excluding 1.0–1.5 cm in the cranio-caudal direction depending on the movement of the target while breathing. Postoperative IMRT was administered to all patients with a median total dose of 50.4 Gy (range, 37.8–50.4 Gy) by conventional fractionation (1.8–2.0 Gy/fraction). The treatment interval between surgery and radiotherapy was 3.7 months (range, 0.9–20.5 months). The doses to the organs at risk were limited per their respective tolerances. The dosimetric parameters of radiation therapy are summarized in Table 2.

Concurrent chemotherapy was regarded as a standard treatment for pancreatic cancer without contraindication. For patients who refused CCRT, RT alone could be an alternative treatment modality. Postoperative CCRT was administered to 55 (90.2%) patients and RT alone to 6 (9.8%). The concurrent chemotherapy regimen comprised gemcitabine (GEM) at 800–1000 mg/m^2 weekly for 3 weeks every 28 days (n=48), capecitabine (CAPE) at 1000 mg/m^2 twice daily on Monday to Friday (n=1), or S-1 at 40 mg/m^2 twice daily for 14 days every 21 days (n=6).

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Table 1. Characteristics of the 61 patients who received postoperative radiotherapy.

Characteristic	No. of patients (%)
Sex	
Male	43 (70.5%)
Female	18 (29.5%)
Median age (years)	59 (range: 33–77)
Tumor location	
Head	33 (54.1%)
Body/tail	27 (44.3%)
Both	1 (1.6%)
Median tumor size (cm)*	3 (range: 1.5–7.5)
Pathology	
Adenocarcinoma	59 (96.7%)
Adenosquamous carcinoma	2 (3.3%)
Histologic grade	
Well-moderately	38 (62.3%)
Poorly	22 (36.1%)
Undefined	1 (1.6%)
AJCC stage	
$T_{1–2}N_0M_0$	8 (13.1%)
$T_3N_0M_0$	30 (49.2%)
$T_{1–3}N_1M_0$	23 (37.7%)
Surgery	
Pancreaticoduodenectomy	32 (52.5%)
Distal pancreatectomy	27 (44.3%)
Total pancreatectomy	2 (3.3%)
Radiotherapy	
Concurrent chemoradiotherapy	55 (90.2%)
Radiotherapy alone	6 (9.8%)
Median irradiation dose (Gy)	50.4 (range: 37.8–50.4)
Postoperative RIAC	
Yes	43 (70.5%)
No	18 (29.5%)
CA19-9 pre-radiotherapy (U/mL)	
≤37	30 (49.2%)
>37	22 (36.1%)
Missing data	9 (14.8%)

* The longest diameter of the tumor on the specimen.
AJCC – American Joint Committee on Cancer; CA19-9 – carbohydrate antigen 19-9; RIAC – regional intra-arterial infusion chemotherapy.

Before and/or after RT, sequential adjuvant chemotherapy was recommended for all patients, with systemic chemotherapy in 15 patients (25.9%), RIAC in 1 patient (1.7%), or both of the above in 42 patients (72.4%). For RIAC, a catheter (5-Fr Rosch hepatic catheter, Cook Medical, Bloomington, IN, USA) was inserted using Seldinger's technique into the femoral artery, and the catheter position was confirmed using digital subtraction angiography. A combination of GEM 1000 mg/m^2, oxaliplatin (OXA) 100 mg/m^2, and 5-fluorouracil (FU) 500 mg/m^2 was injected via the celiac artery and the superior mesenteric artery by 2/3 and 1/3 of the dosage, respectively. Postoperative RIAC was administered to 43 patients in total, and 41 and 17 patients before and after RT, respectively, repeated every 4 to 6 weeks with a median cycle of 3 (range, 1–8).

For patients who underwent systemic chemotherapy, S-1 and GEM-based systemic chemotherapy were recommended to patients based on physicians' decisions, including GEM 1000 mg/m^2 weekly for 3 weeks every 28 days (n=32); OXA 100 mg/m^2 on day 1 plus GEM 1000 mg/m^2 on days 1 and 8 every 21 days (n=12); albumin-bound paclitaxel 125 mg/m^2 plus GEM 1000 mg/m^2 on days 1, 8, and 15 (n=3), every 28 days; and S-1 at 40 mg/m^2 twice daily for 14 days every 21 days (n=10).

Follow-up and statistical analysis

Patients were followed up weekly by physical examination, complete blood counts, and hepatic function testing during irradiation and approximately every 3 months after irradiation. In addition, radiological studies were examined on each follow-up visit and required if abdominal or back pain or other symptoms suggestive of local recurrence and distant metastases occurred. We used the Common Terminology Criteria for Adverse Events version 3.0 to assess the treatment-related toxicities. The efficacy endpoints were overall survival (OS) and disease-free survival (DFS). Observation for all endpoints was started at the commencement of surgery and ended when an event of interest occurred or at the last follow-up.

The OS and DFS were calculated using the Kaplan-Meier method. Comparison of survival between different subgroups was conducted using the log-rank test in univariate analysis. Then, variables with P<0.20 in univariate analysis along with another plausible covariate, tumor size, were included in multivariable analysis using Cox's proportional hazard model. This probability level was chosen to incorporate all potentially important predictor variables in the final modeling process. Data analyses were conducted using STATA statistical software version 11.0 (Stata Corporation, College Station, TX, USA). P value ≤0.05 was considered statistically significant.

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Table 2. Dosimetric parameters of radiotherapy for the organs at risk.

Organ	Dosimetric parameter	Mean ±SD
Left kidney	Dmean (Gy)	11.66±2.46
Right kidney	Dmean (Gy)	11.23±2.94
Liver	Dmean (Gy)	11.55±3.97
Stomach	Dmax (Gy)	50.42±4.47
	V50 (%)	1.88±2.63
Duodenum	Dmax (Gy)	51.27±3.25
	V50 (%)	12.69±13.61
Spinal cord	Dmax (Gy)	36.47±6.66

SD – standard deviation; V50 – percentage of volume receiving more than 50 Gy.

Table 3. Frequencies of treatment-related adverse event categories by NCI-CTC in 61 patients.

	No. of patients				
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Nausea/vomiting	39	12	7	3	0
Diarrhea/constipation	54	4	3	0	0
Leucopenia	10	18	20	12	1
Neutropenia	20	14	17	8	2
Anemia	17	33	10	0	1
Thrombocytopenia	35	11	15	0	0
Abnormal liver function	52	7	2	0	0

NCI-CTC – National Cancer Institute Common Toxicity Criteria.

Results

Tolerance and toxicity

Overall, the patients tolerated the combination of RT and chemotherapy well, except for 4 patients in whom RT was terminated after 37.8–48.6 Gy (because of Grade IV leucopenia/anemia in 2 patients, abdominal pain in 1 patient, and liver metastasis in 1 patient). Grades 0, 1, 2, 3, and 4 toxicities occurred in 6.6% (4/61), 16.4% (10/61), 47.5% (29/61), 24.6% (15/61), and 4.9% (3/61) of patients, respectively, and no treatment-related deaths were observed. The incidence of Grades 0, 1, 2, and 3 non-hematological toxicity was 57.4% (35/61), 21.3% (13/61), 16.4% (10/61), and 4.9% (3/61), respectively. For hematological toxicity, the incidence of Grades 0, 1, 2, 3, and 4 events were 8.2% (5/61), 24.6% (15/61), 42.6% (26/61), 19.7% (12/61), and 4.9% (3/61), respectively. The treatment-related adverse events are summarized in Table 3.

Survival in the overall cohort

Until the last follow-up at January 2017, 19 patients were alive, and the other 42 had died. The median follow-up period for all patients was 25.5 months (range, 4.9–59.7 months), and 38.3 months (range, 10.5–59.7 months) for alive or censored patients. The median OS time was 27.4 months (95% confidence interval [CI], 21.3–33.5 months), and the OS rates were 86.9%, 31.0%, and 21.7% at 1, 3, and 5 years, respectively (Figure 1).

Forty-five patients had disease recurrence after surgery (median 15.8 months, range 4.2–54.2 months), including 8 (17.8%) with local recurrence alone, 23 (51.1%) with distant metastases alone, and 14 (31.1%) with both local and distant failures. The median DFS time was 16.7 months (95% CI, 13.1–24.7 months), with DFS rates of 72.3%, 16.1% and 0% at 1, 3, and 5 years, respectively (Figure 1).

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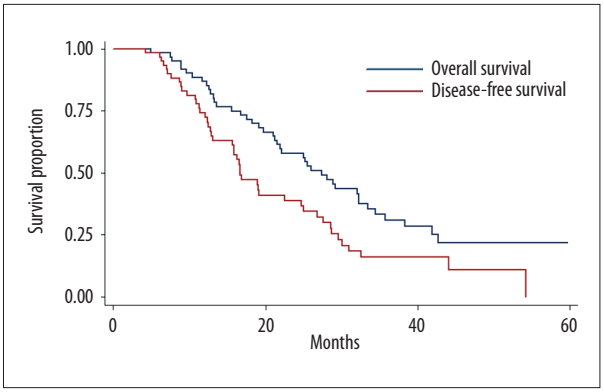

Figure 1. Kaplan-Meier estimates of overall survival and disease-free survival in 61 patients with pancreatic carcinoma treated by postoperative intensity-modulated radiotherapy in combination with regional intra-arterial infusion chemotherapy and systemic chemotherapy.

Prognostic factors

In univariate analysis, administration of postoperative RIAC in pancreatic carcinoma significantly improved OS and DFS when compared to control ($p<0.05$) (Table 4). It was confirmed as an independent favorable prognostic factor for OS and DFS in multivariate analyses (hazard ratio [HR] 3.25, 95% CI 1.03–10.26, p=0.044; HR 4.52, 95% CI 1.18–17.29, p=0.027) (Table 5). Furthermore, in multivariate analysis, the independent favorable prognostic factor was CCRT for OS (HR 8.38, 95% CI 1.12–62.77, p=0.039). Univariate and multivariate analyses also indicated that a favorable prognostic factor for DFS was pre-radiotherapy CA19-9 level ≤37 U/mL (HR 2.73, 95% CI 1.30–5.76, p=0.0080).

Table 4. Univariate analysis for prognostic factors in the 61 patients.

Variable	Category	n	Median OS	p Value	Median DFS	p Value
Sex	Male	43	27.4		16.7	
	Female	18	28.1	0.78	19.2	0.68
Age (years)	≤59	32	32.0		16.9	
	>59	29	21.9	0.15	16.3	0.46
Location	Head	33	29.2		19.1	
	Neck/tail	27	21.9	0.62	16.5	0.76
Histologic grade	Well-moderately	38	28.9		16.9	
	Poorly	22	25	0.92	16.3	0.76
	Undefined	1				
Tumor Size (cm)	≤3	29	28.9		18.9	
	>3	27	28.1	0.22	16.7	0.50
	Missing	5				
Lymph node metastasis	No	38	28.1		18.9	
	Yes	23	25.5	0.53	15.6	0.17
Concurrent chemotherapy	Yes	55	27.4		16.9	
	No	6	11.7	0.12	12.5	0.070
Postoperative RIAC	Yes	43	29.2		19.2	
	No	18	17.5	0.0075	12.9	0.0078
CA19-9 pre-radiotherapy	≤37	30	28.9		24.7	
	>37	22	25.0	0.12	16.5	0.019
	Missing	9				

OS – overall survival; DFS – disease-free survival; RIAC – regional intra-arterial infusion chemotherapy; CA19-9 – carbohydrate antigen 199.

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Table 5. Multivariate analysis of factors affecting overall survival and disease-free survival.

Variable	Category	OS HR (95% CI)*	p value	DFS HR (95% CI)	p value
CCRT	Yes No	8.38 (1.12–62.77)	0.039		
Postoperative RIAC	Yes No	3.25 (1.03–10.26)	0.044	4.52 (1.18–17.29)	0.027
CA19-9 pre-radiotherapy	≤37 >37			2.73 (1.30–5.76)	0.0080

CI – confidence interval; HR – hazard ratio; OS – overall survival; DFS – disease-free survival; CCRT – concurrent chemotherapy; RIAC – regional intra-arterial infusion chemotherapy; CA19-9 – carbohydrate antigen 199. * HR >1 indicates an increased risk of death for the second level of the variables listed.

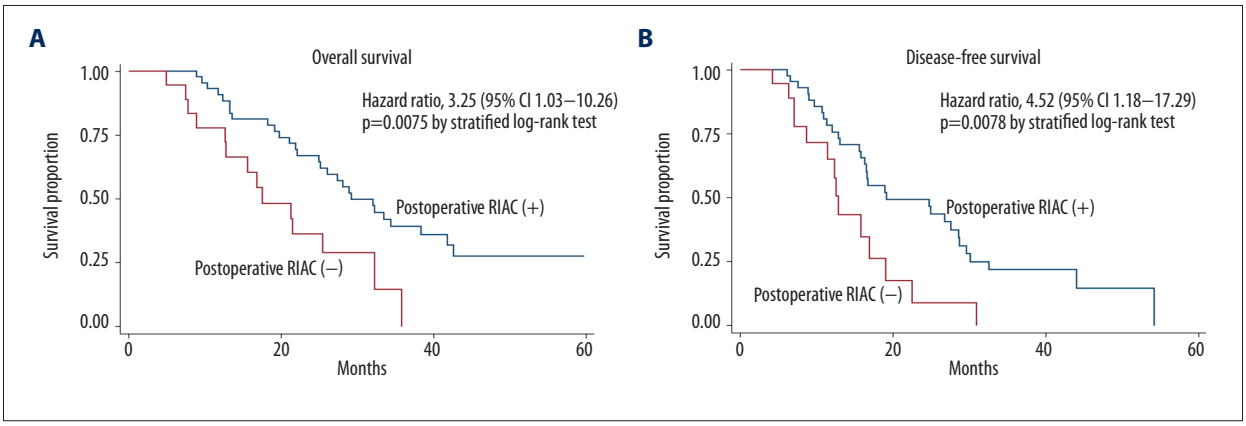

Figure 2. Kaplan-Meier plots of overall survival and disease-free survival stratified by independent prognostic factor postoperative regional intra-arterial infusion chemotherapy (RIAC). (**A**) Shows overall survival. (**B**) Shows disease-free survival.

Survival based on postoperative RIAC

The correlations of postoperative RIAC with OS and DFS are shown in Figure 2. Patients who received postoperative RIAC had a significantly improved OS rate (90.6% at 1 year and 39.1% at 3 years), compared to the patients who did not (72.2% at 1 year and 0% at 3 years). The median OS times were 29.2 and 17.5 months in patients with or those without postoperative RIAC, respectively (Figure 2A). DFS was also significantly longer in patients receiving postoperative RIAC (75.6% at 1 year and 21.7% at 3 years) compared to patients not receiving postoperative RIAC (64.8% at 1 year and 0% at 3 years). The median DFS times were 19.2 and 12.9 months for patients with or those without postoperative RIAC, respectively (Figure 2B).

Survival based on CCRT

Patients who received CCRT had longer OS than those with RT alone. Moreover, the CCRT group showed longer median OS time (27.4 *vs.* 11.7 months) and higher 1- and 3-year OS rates (89.1% and 32.9% *vs.* 50.0%, and 0%, respectively) than the RT group. Patients who received CCRT tended to have better DFS than who received RT alone, with a median DFS time and 1- and 3-year DFS rates of 16.9 months, 73.2%, and 17.3%, respectively, for the CCRT group, compared to 12.5 months, 66.7%, and 0%, respectively, for the RT group (p=0.070). However, statistical significance was not confirmed in multivariate analysis (HR 1.56, 95% CI 0.15–16.20, p=0.71).

Discussion

Pancreatic carcinoma is among the most fatal cancers worldwide. Despite the poor prognosis after surgery, surgical resection remains the sole curative modality for pancreatic carcinoma. Postoperative adjuvant chemotherapy has been widely applied, but whether RT combined with chemotherapy would further improve prognosis remains controversial, although it has been proved to be effective even in rare malignancies [15]. As a result, we performed this study to investigate the efficacy and toxicities of postoperative RT in resected pancreatic carcinoma patients.

In our study, all the patients tolerated combination RT and chemotherapy very well, despite the fact that 90.2% of patients received CCRT, which induces more toxicity compared

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to RT alone in patients with pancreatic carcinomas [16]. The treatment-related toxicity of CCRT or RT was mild for most patients, and there were no Grade 4 non-hematologic toxicities, which is consistent with the results of another study [17], and better than those of a study on non-small cell lung cancer after CCRT [18].

Reports have not yet confirmed the role of either postoperative RT or CCRT as a prophylactic measure for pancreatic carcinoma after resection. The ESPAC phase III clinical trial showed that postoperative RT resulted in decreased survival, with a median OS of 15.9 months in the RT group, and 17.9 months in the control group ($p \leq 0.05$) [9]. A meta-analysis of 5 prospective trials also indicated that CCRT is not an effective adjuvant treatment in comparison with chemotherapy alone for resected pancreatic carcinomas patients [19]. However, in a prospective randomized phase III trial, the median OS for pancreatic cancer patients received adjuvant CCRT was significantly longer than that of the control group (20 months *vs.* 11 months, p=0.04) [20]. In a recently published SEER analysis on postoperative radiotherapy, Mellon et al. reported a median survival time and 1- and 3-year OS rates of 21 months, 77%, and 28%, respectively, for patients with pancreatic carcinoma after surgery, chemotherapy, and postoperative radiotherapy, compared to 20 months, and 70%, and 25%, respectively for patients without RT (p=0.02) [21]. In a Mayo Clinic study on postoperative radiotherapy, Corsini et al. reported a median OS time of 25.2 months and a 5-year OS rate of 28% in patients with pancreatic carcinoma after postoperative radiotherapy, compared to 19.2 months and 17%, respectively, in patients without RT (p=0.001) [10]. Our data support the results of the Mayo Clinic analysis and reveal similar survival benefits for the entire group after surgical resection and postoperative radiotherapy.

Nevertheless, the Mayo Clinic study and our study illustrate an advantageous outcome for patients after postoperative RT, especially for the 98% and 90.2% of patients who received concurrent chemotherapy. In our study, CCRT was confirmed by multivariate analysis as a factor for improved OS compared to RT alone. Therefore, we believe that in the absence of associated toxicities, the concurrent addition of RT to systemic chemotherapy would further improve the outcomes, especially for effective regimens such as GEM/CAPE/S-1 [22–24]. According to the results of our study, CCRT with gemcitabine could be recommended as an optional treatment for patients with resected pancreatic carcinoma and exhibiting a good performance status.

The incidence of disease failure in resected pancreatic carcinoma is high, with approximately 70% to 85% of patients with pancreatic carcinoma having distant metastases after surgery, even among early-stage patients [25,26]; therefore, systemic chemotherapy plays an important role in disease control. In a randomized phase III study, postoperative adjuvant GEM was associated with better DFS in patients with pancreatic carcinoma [5]. However, it remains undetermined whether combining RT with chemotherapy could improve DFS [27]. In a retrospective study evaluating the role of adjuvant FU-based CCRT in pancreatic carcinoma after resection, the DFS time was disappointing, with a median DFS of 10 months [28]. In contrast, an improved DFS (12 months) was observed in the EORTC phase II trial, in which GEM was administered concurrently with maintenance RT [7]. In a more recent study retrospectively analyzing 62 patients with resected pancreatic carcinoma treated with FU-based or GEM-based CCRT, the median DFS was 15.4 months, with 1-year and 2-year DFS rates of 58.1% and 38.5%, respectively [29]. In the present study, similar DFS benefits for the entire group were observed. These results are encouraging, especially considering that fewer patients received CCRT in our study compared to the above study (90.2% *vs.* 100%), although statistical significance in DFS time and 1- and 2-year DFS rates between the CCRT and RT groups was not reached.

One difference between our study and other studies was the use of RIAC as an option for the management of pancreatic carcinoma. Theoretically, RIAC could improve disease control for patients with pancreatic carcinoma by delivering high concentrations of chemotherapeutic agents to the tumor bed and liver, and it did not increase the toxicity when compared to systemic chemotherapy [12]. However, there is no consensus on the benefit of this therapy [12–14]. For example, some studies have reported improved survival in patients with resectable pancreatic carcinoma and reduced risk of liver metastasis [12,13]. In contrast, a prospective randomized controlled trial did not demonstrate the survival and local control benefit of adjuvant RIAC and RT after surgery in patients with pancreatic carcinoma [14]. Our study showed OS and DFS improvement by adding postoperative RIAC as part of the adjuvant therapy. However, the benefit of RIAC for pancreatic carcinoma needs to be interpreted with caution, because the retrospective nature of this study and the small number of included patients.

CA19-9 is the best tumor marker for the diagnosis of pancreatic carcinoma and monitoring patients after treatment. A few studies have shown that the serum CA19-9 value is an independent predictor of survival after resection [30,31]. In the RTOG 9704 study, postoperative serum CA-199 levels that were more than the dichotomized cutoff values of 180 U/mL and 90 U/mL were unfavorable predictors for OS in resected pancreatic carcinoma patients who underwent adjuvant chemoradiotherapy [31]. Our data, however, demonstrated that the postoperative pre-RT CA19-9 level was not an independent predictor of OS, and we defined a cutoff value of 37 U/mL as the upper limit of normal. When the cutoff value was set to 200 U/mL in our study, pre-RT serum CA19-9 level ≤200 U/

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mL was significantly associated with a better OS ($p<0.05$) in univariate analysis, with a median OS time of 28.9 months. It seems that using a cutoff value of CA19-9 much more than the upper limit of normal might be reasonable when determining prognostic significance. Given the small sample of included patients with pre-RT CA19-9 level >200 U/mL, we did not use that cutoff value for further analysis. However, our study showed that a postoperative pre-RT CA19-9 value of ≤37 U/mL was an independent favorable predictor for longer DFS in univariate and multivariate analyses. This result is consistent with that reported in the literature, which showed that postoperative CA19-9 values of ≤37 U/mL in patients with pancreatic carcinoma after surgery and adjuvant therapy was correlated with a better DFS, regardless of their initial CA 19-9 level [32].

Conclusions

CCRT was associated with a better OS than RT in patients with resected pancreatic carcinoma and was tolerated well. Furthermore, adding RIAC to RT or CCRT was associated with improved OS and DFS. CCRT and postoperative RIAC were favorable prognostic predictors of OS; pre-RT CA19-9 level ≤37 U/mL and postoperative RIAC were favorable prognostic predictors of DFS. We propose that postoperative RT should be one of the treatment options for these patients, but that it should be administered concurrently with chemotherapy. We also recommend that RIAC be integrated into the treatment regimen. As our study was retrospective in nature, with a limited number of patients, a prospective clinical trial is needed to clarify the best treatment options.

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Conflicts of Interest

The authors declare that there are no conflicts of interest.

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