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Is There a Potential Oncologic Role for Local Therapy on Hepatic Metastasis in Patients Who Undergo Curative Pancreatectomy for Pancreatic Cancer?

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Purpose: In pancreatic cancer, therapeutic investigations targeting liver metastases could improve survival. However, the use of local treatment for oligometastasis in pancreatic cancer remains controversial. This study aimed to investigate the oncological role of local therapy in patients who underwent curative pancreatectomy and subsequently developed liver metastases.

Materials and Methods: Data concerning patients who underwent curative pancreatectomy for pancreatic cancer at Severance Hospital in Seoul, South Korea between 2006 and 2018 were retrospectively reviewed. We included patients with one or two liver metastases, as confirmed on imaging. We excluded those with metastases in other organs. The patients were divided into two groups: the NT group, receiving conventional therapy without local treatment; and the LT group, receiving local treatments for liver metastases alongside standard therapy.

Results: Of the 43 included patients (NT group, n=33; LT group, n=10), no significant differences were observed in overall survival (OS) [hazard ratio (HR) 0.846; 95% confidence interval (CI) 0.397–1.804; p=0.665] or post-recurrence survival (HR 0.932; 95% CI 0.437–1.985, p=0.855) between the two groups. In multivariate analysis, early recurrence within 6 months (p<0.001) and the use of 5-fluorouracil (FU)-based adjuvant chemotherapy (CTx) (p=0.011), as well as 5-FU-based CTx after liver metastasis (p=0.008) when compared with gemcitabine-based regimens, were significant predictors of poor OS.

Conclusion: The oncologic role of local treatment for hepatic metastasis remains controversial in patients with hepatic metastasis after radical pancreatectomy. In the era of potent chemotherapeutic regimens, further research is needed to clarify the efficacy of such regimens.

Key Words: Hepatic metastasis, pancreatectomy, pancreatic neoplasms, radiofrequency ablation

INTRODUCTION

In the United States, pancreatic ductal adenocarcinoma (PDAC) is estimated to be the 10th most commonly diagnosed cancer, but the 4th leading cause of cancer death.[1] At the time of diagnosis, <20% of PDAC cases are diagnosed sufficiently early for upfront surgical resection.[2,3] Even with radical resection, PDAC recurs frequently, and the 5-year survival rate is only approximately 20%.[4,5] Various treatments have been proposed, and multiple studies have been conducted in relation to this disease.[6]

Metastases commonly occur in the liver in most malignancies, especially in pancreatic cancer. Of patients with pancreatic cancer, >50% have liver metastases at the time of diagnosis.[7] Following radical pancreatectomy, hepatic metastasis remains a prevalent characteristic of PDAC.[8,9] Effective therapeutic investigations aimed at liver metastases hold the potential to enhance survival outcomes for patients with pancreatic cancer. Several studies have examined local treatment for postoperative hepatic oligometastasis in various cancer types.[10,11]

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Research results in relation to pancreatic cancer remain controversial, with further research warranted.[12] The current study aimed to evaluate the potential oncological role of local treatment among patients who had undergone curative pancreatectomy and subsequently developed liver oligometastases.

MATERIALS AND METHODS

Study design and patient selection

We conducted a retrospective review of patient data from Severance Hospital in South Korea, focusing on individuals who had undergone curative pancreatectomy for pancreatic cancer between 2006 and 2018 (Fig. 1). We selected patients with an American Society of Anesthesiologists physical status (ASA PS) score ≤3 at the time of surgery who had received postoperative adjuvant chemotherapy (CTx). Additionally, patients with one or two liver metastatic lesions after surgery, as confirmed on computed tomography (CT) and magnetic resonance imaging scans, were included in the study. Patients with metastases in organs other than the liver at the time of initial metastasis detection were excluded. We divided the patients into two groups: NT group, who continued to receive conventional treatment without local treatment; and LT group, who received local treatments for metastatic liver lesions and standard therapy. This study received approval from the Institutional Review Board of Severance Hospital (IRB 4-2023-1482).

Our primary outcome was overall survival (OS), defined as the time from curative pancreatectomy to the date of death from any cause. Patients who were alive at the last follow-up or lost to follow-up were censored at their last known follow-up date. The secondary outcome was post-recurrence survival (PRS), measured from the time of recurrence detection, typically confirmed on follow-up CT scans, to the date of death from any cause. Baseline characteristics were summarized using descriptive statistics. Continuous variables were compared using a Wilcoxon rank sum test, while categorical variables were analyzed using Fisher's exact test. Survival analyses were conducted using a Cox proportional hazards model and Kaplan–Meier estimates. All statistical analyses were performed using IBM SPSS version 23.0 (IBM Corp., Armonk, NY, USA) and SAS Studio, version 3.8 (SAS Institute Inc., Cary, NC, USA). A p-value<0.05 indicated statistical significance.

RESULTS

Patient screening

Between 2006 and 2018, 556 patients underwent curative pancreatectomy for PDAC at Severance Hospital (Fig. 1). Of these, 420 patients had an ASA PS score ≤3 and received postoperative adjuvant CTx. Among them, 43 patients developed hepatic oligometastasis, characterized as having 1–2 liver lesions, with no metastases to other organs. NT group comprised 33 patients, while LT group comprised 10 patients, of whom nine patients had undergone radiofrequency ablation (RFA) and one pa-

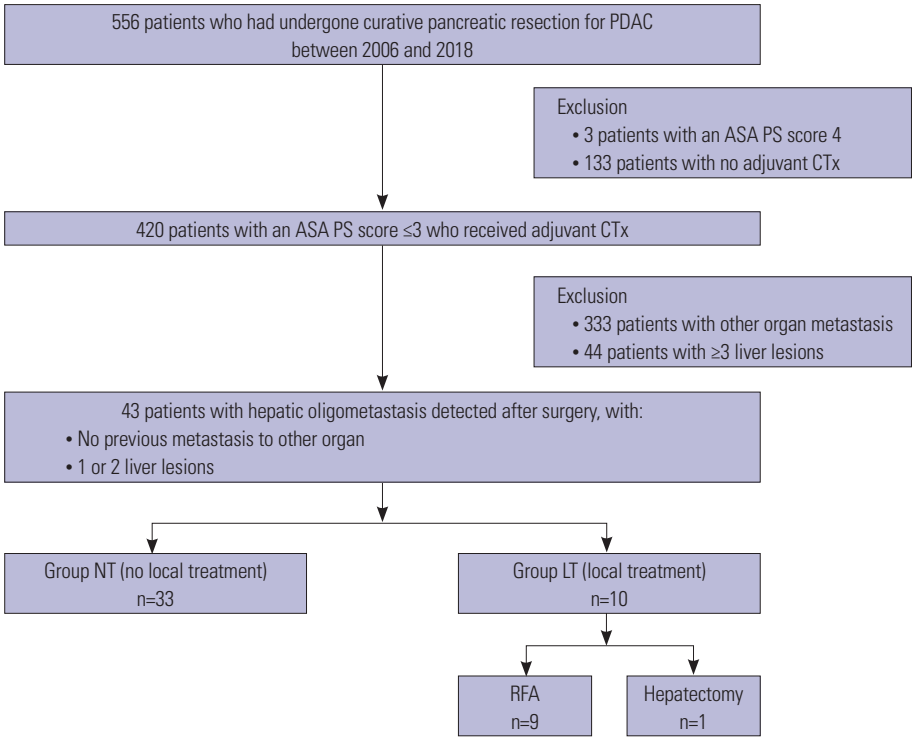

Fig. 1. Flowchart of the study population. ASA PS, American Society of Anesthesiologists physical status; CTx, chemotherapy; PDAC, pancreatic ductal adenocarcinoma; RFA, radiofrequency ablation.

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tient had undergone hepatectomy.

General characteristics of the experimental group (LT group)

The clinicopathological characteristics of LT group are summarized in Table 1. LT group patients comprised three male and seven female [median age at the time of surgery, 65 years (range, 57–71 years)]. Six patients underwent pylorus-preserving pancreaticoduodenectomy (PPPD), and four underwent distal pancreatectomy (DP). Three patients had laparoscopic surgery, while the remainder underwent open surgery. Pathology findings indicated that eight patients exhibited moderate cell differentiation, while one showed good cell differentiation. One patient had nearly complete tumor cell necrosis after neoadjuvant CTx. Lymphovascular invasion (LVI) was observed in two patients, and perineural invasion (PNI) was observed in six patients. One patient had a surgical margin as close as 50 μm. Except for one tumor cell necrosis case, the median tumor size was 2.0 cm, and the tumor size ranged from 1.6 cm to 2.7 cm. Four patients received neoadjuvant CTx. As a local treatment, nine patients underwent RFA, and one patient underwent a right anterior resection of the liver.

Comparison between NT and LT groups

The median ages in NT and LT groups were 63.67 years and 65.10 years, respectively (Table 2). No significant difference in sex distribution was observed between the two groups (p=0.480). Compared to NT group, the body mass index (BMI) values were significantly higher in LT group (p=0.048), as were the ASA PSs (p=0.004). A significant difference was also observed in tumor size and T stage (p=0.006 and p=0.041, respectively). However, no significant differences were observed in the tumor location, liver metastasis lesion size, or the number of metastases.

LT group had a higher rate of neoadjuvant CTx (40%) compared with NT group (12.12%), but this difference was not statistically significant (p=0.070). However, a significant difference was observed in terms of type of neoadjuvant regimen used between the groups (p=0.046). NT group received FOLFIRINOX-based or 5-fluorouracil (FU)-based regimens, whereas LT group received gemcitabine-based or Xeloda-based neoadjuvant CTx. Adjuvant CTx regimens were similar between the groups (p=0.324). After the development of liver metastasis, no significant difference was observed in the CTx regimens used between the two groups (p=0.120).

Independent factors affecting long-term survival

In Table 3, early recurrence within 6 months was significantly associated with OS [hazard ratio (HR) 18.500; 95% confidence interval (CI) 5.474–62.519; p<0.001]. Regarding adjuvant CTx regimens, patients receiving 5-FU-based regimens had a significantly higher HR for OS (HR 3.263; 95% CI 1.296–8.215; p=0.012) compared to those receiving gemcitabine-based thera-

Table 1. Baseline Characteristics of Patients Who Received LT

No	Sex	Age (yr)	ASA	Surgery*	Location of tumor	Tumor size (cm)	Pathology	TNM stage†	Cell differentiation	Retrieved LN	Positive LN	LVI	PNI	Margin status	Neoadjuvant CTx regimen	1st line adjuvant CTx regimen	CTx regimen after recurrence	Local treatment
1	M	57	1	PPPD	Head	0.0	PDAC	T1N0M0	Necrosis‡	20	0	Negative	Negative	Negative	Gemcitabine+ Cisplatin+RTx	Gemcitabine+ Cisplatin	5FU+ Paclitaxel	RFA
2	F	64	1	DP	Tail	2.5	PDAC	T2N1M0	Well	37	1	Negative	Positive	Negative	-	Gemcitabine+ Capecitabine	FOLFOX	RFA
3	F	63	1	PPPD	Neck	2.0	PDAC	T1N1M0	Moderate	11	2	Negative	Negative	Positive§	-	Gemcitabine+ RTx	Gemcitabine+ Capecitabine	RFA
4	F	58	1	DP	Body	2.0	PDAC	T1N1M0	Moderate	23	2	Negative	Positive	Negative	-	Gemcitabine+ RTx	Gemcitabine+ Cisplatin	RFA
5	F	68	2	PPPD	Head	1.6	PDAC	T1N0M0	Moderate	3	0	Negative	Negative	Negative	Gemcitabine+ RTx	Gemcitabine	Gemcitabine+ Cisplatin	RFA
6	F	66	1	DP	Body	1.6	PDAC	T1N1M0	Moderate	14	1	Negative	Negative	Negative	-	Gemcitabine+ RTx	Gemcitabine+ Erlotinib	RFA
7	M	71	3	PPPD	Head	2.0	PDAC	T2N1M0	Moderate	18	1	Negative	Positive	Negative	Capecitabine+RTx	Gemcitabine	Capecitabine	RFA
8	M	63	2	PPPD	Head	2.3	PDAC	T2N0M0	Moderate	21	0	Positive	Positive	Negative	-	Gemcitabine	Gemcitabine+ Erlotinib	RFA
9	F	70	2	DP	Body	2.0	PDAC	T1N1M0	Moderate	20	1	Negative	Positive	Negative	Gemcitabine+ RTx	Gemcitabine+ Erlotinib	FOLFIRINOX	RFA
10	F	71	2	PPPD	Head	2.7	PDAC	T2N1M0	Moderate	19	3	Positive	Positive	Negative	-	FOLFIRINOX	Gemcitabine+ Erlotinib	Segmentectomy

ASA, American Society of Anesthesiologists; CTx, chemotherapy; DP, distal pancreatectomy; F, female; FU, fluorouracil; LN, lymph node; LT, local therapy; LVI, lymphovascular invasion; M, male; PDAC, pancreas ductal adenocarcinoma; PNI, perineural invasion; PPPD, pylorus preserving pancreaticoduodenectomy; RFA, radiofrequency ablation; RTx, radiotherapy; TNM, tumor, node, metastasis.
*Nos. 4, 6, and 10 underwent laparoscopic surgery; †The 8th edition of the American Joint Committee on Cancer staging system; ‡No.1, near total necrosis of tumor cells; §No.3., margin status RPM 50 μm.

Table 2. Comparison between NT and LT Groups

Variables	NT group (n=33)	LT group (n=10)	*p*-value
Age (yr)	63.67±9.28	65.1±5.04	0.561
Male	15 (45.50)	3 (30)	0.480
BMI (kg/m^2)	22.73±2.04	24.61±3.76	0.048
ASA PS			0.004
1	2 (6.06)	5 (50)	
2	21 (63.64)	4 (40)	
3	10 (30.3)	1 (10)	
Tumor location			0.584
Head/uncinate	19 (57.58)	5 (50)	
Neck	1 (3.03)	1 (10)	
Body	5 (15.15)	3 (30)	
Tail	5 (15.15)	1 (10)	
Body+tail	3 (9.09)	0 (0)	
Tumor size (cm)	2.70 (0.60–7.00)	2.00 (0.00–2.70)	0.006
Resectability			0.362
Resectable	28 (84.85)	7 (70)	
Borderline resectable	5 (15.15)	3 (30)	
CA 19-9 (U/mL)			
Pre-operative	270.19 (0.80–2409.00)	208.50 (0.10–1196.00)	0.702
Recurrent	71.00 (0.10–3180.00)	119.90 (0.10–3140.00)	0.356
Operation type			>0.999
PD	20 (60.61)	6 (60)	
DP	13 (39.39)	4 (40)	
R0 resection	26 (78.79)	9 (90)	0.656
LVI	14 (42.42)	2 (20)	0.276
PNI	25 (75.76)	6 (60)	0.427
Early recurrence			
Within 6 months	11 (33.33)	1 (10)	0.237
Within 1 year	25 (75.76)	7 (70)	0.698
TNM stage			
T stage			0.041
T1	7 (21.21)	6 (60)	
T2	19 (57.58)	4 (40)	
T3	7 (21.21)	0 (0)	
N stage			0.392
N0	14 (42.42)	3 (30)	
N1	16 (48.48)	7 (70)	
N2	3 (9.09)	0 (0)	
Neoadjuvant CTx	4 (12.12)	4 (40)	0.070
Neoadjuvant regime			0.046
Gemcitabine base	0 (0)	3 (30)	
Xeloda base	0 (0)	1 (10)	
5-FU base	2 (6.06)	0 (0)	
FOLFIRINOX base	2 (6.06)	0 (0)	
Adjuvant regime			0.324
Gemcitabine base	22 (66.67)	9 (90)	
Xeloda base	3 (9.09)	0 (0)	
5-FU base	6 (18.18)	0 (0)	
FOLFIRINOX base	2 (6.06)	1 (10)	
CTx after liver metastasis regime			0.120
Gemcitabine base	14 (42.42)	6 (60)	
Xeloda base	0 (0)	1 (10)	
5-FU base	2 (6.06)	2 (20)	
FOLFIRINOX base	11 (33.33)	1 (10)	
Others	6 (18.18)	0 (0)	
Liver metastasis lesion			
No. of metastatic tumor			>0.999
1	23 (69.7)	7 (70)	
2	10 (30.3)	3 (30)	
Largest lesion size (cm)	1.40 (0.50–2.80)	1.35 (0.70–3.00)	0.620

ASA PS, American Society of Anesthesiologists physical status; BMI, body mass index; CA, carbohydrate antigen; CTx, chemotherapy; DP, distal pancreatectomy; FU, fluorouracil; LVI, lymphovascular invasion; PD, pancreaticoduodenectomy; PNI, perineural invasion; TNM, tumor, node, metastasis.
Data are presented as mean±standard deviation, median (range), or n (%).

pies. Concerning CTx after liver metastasis, the HR for 5-FU-based CTx compared to gemcitabine-based was higher at 2.739, but it did not reach statistical significance (p=0.080). However, the FOLFIRINOX regimen significantly improved OS (HR 0.350; 95% CI 0.145–0.847; p=0.020).

In Table 4, the multivariate analysis confirmed that early recurrence within 6 months remained a significant predictor of poor OS (HR 18.485; 95% CI 4.933–69.262; p<0.001). Regarding adjuvant regimens, patients receiving 5-FU-based therapy had a significantly higher HR (HR 4.775; 95% CI 1.436–15.880; p=0.011) compared to those receiving gemcitabine-based therapy. In contrast to univariate analysis, for CTx after liver metastasis, 5-FU-based therapy was associated with a significantly higher HR (HR 5.397; 95% CI 1.543–18.885; p=0.008), while FOLFIRINOX did not show a significant effect (p=0.282).

Oncologic effect of local treatment for hepatic metastasis in resected pancreatic cancer

In Table 5, no significant differences in OS were observed according to Cox hazard regression analysis (HR 0.846; 95% CI 0.397–1.804; p=0.665), and similar results were observed in Kaplan–Meier curves, as shown in Fig. 2 (p=0.665). Furthermore, when PRS was defined from the date of recurrence rather than the date of surgery, both Cox hazard regression analysis (HR 0.932; 95% CI 0.437–1.985; p=0.855) and Kaplan–Meier curves (p=0.854) indicated no significant differences in survival outcomes (Fig. 3). Table 5 includes adjusted analyses, with the adjustment variables being N (node) stage, adjuvant CTx regimen, CTx after the liver metastasis regime, and early recurrence rate (within 6 months), all of which showed significance in the multivariate analysis (Table 4). In the adjusted

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Table 3. Univariate Analysis of Variables in Relation to Patient OS

Variables	HR	Exp (B) (95% CI)	*p*-value
Age (yr) continuous	1.027	0.985–1.071	0.207
Sex			
Male	(Ref)		
Female	0.958	0.487–1.884	0.902
BMI (kg/m^2) continuous	1.038	0.904–1.191	0.600
ASA PS			
1	(Ref)		
2	0.807	0.341–1.909	0.625
3	0.663	0.240–1.834	0.428
Tumor location			
Head/uncinate	(Ref)		
Neck	2.361	0.533–10.466	0.258
Body	1.009	0.436–2.336	0.983
Tail	1.515	0.599–3.832	0.381
Body+tail	0.893	0.205–3.882	0.880
Tumor size (cm) continuous	1.164	0.853–1.589	0.337
Resectability			
Resectable	(Ref)		
Borderline resectable	1.108	0.483–2.541	0.808
CA 19-9 (U/mL) continuous			
Pre-operative	0.999	0.998–1.001	0.351
Recurrent	1.000	1.000–1.001	0.310
Operation type			
DP	(Ref)		
PD	0.937	0.484–1.816	0.847
R status			
R0	(Ref)		
R1	1.046	0.455–2.408	0.915
LVI	1.596	0.800–3.187	0.185
PNI	0.918	0.441–1.909	0.818
Early recurrence			
Within 6 months	18.500	5.474–62.519	<0.001
Within 1 year	1.921	0.894–4.129	0.094
TNM stage			
T stage			
T1	(Ref)		
T2	1.167	0.559–2.435	0.681
T3	1.363	0.507–3.661	0.539
N stage			
N0	(Ref)		
N1	1.867	0.911–3.830	0.088
N2	0.306	0.040–2.346	0.254
Neoadjuvant CTx	0.688	0.285–1.659	0.405
Neoadjuvant regime			
Gemcitabine base	(Ref)		
Xeloda base	2.412	0.173–33.566	0.512
5-FU base	2.243	0.262–19.176	0.461
FOLFIRINOX base	0.880	0.079–9.773	0.917
Adjuvant regime			
Gemcitabine base	(Ref)		
Xeloda base	1.919	0.561–6.562	0.299
5-FU base	3.263	1.296–8.215	0.012
FOLFIRINOX base	1.029	0.241–4.399	0.970
CTx after liver metastasis regime			
Gemcitabine base	(Ref)		
Xeloda base	1.465	0.190–11.278	0.714
5-FU base	2.739	0.886–8.470	0.080
FOLFIRINOX base	0.350	0.145–0.847	0.020
Others	1.236	0.458–3.330	0.676
Liver metastasis lesion			
No. of metastatic tumor			
1	(Ref)		
2	1.135	0.557–2.311	0.727
Largest lesion size (cm) continuous	0.997	0.579–1.718	0.991

ASA PS, American Society of Anesthesiologists physical status; BMI, body mass index; CA, carbohydrate antigen; CI, confidence interval; CTx, chemotherapy; DP, distal pancreatectomy; Exp(B), exponential of B; FU, fluorouracil; HR, hazard ratio; LVI, lymphovascular invasion; OS, overall survival; PD, pancreaticoduodenectomy; PNI, perineural invasion; Ref, reference; TNM, tumor, node, metastasis.

analysis, OS (HR 0.387; 95% CI 0.143–1.049; p=0.062) and PRS (HR 0.469; 95% CI 0.181–1.211; p=0.118) also remained non-significant.

DISCUSSION

Pancreatic cancer has a poor prognosis, with only <20% of PDAC cases being diagnosed sufficiently early for upfront surgical resection.[1-3] Metastatic pancreatic cancer has a particularly dismal outcome, and distant metastasis is responsible for approximately 80% of cancer-related deaths.[13] For selected patients with limited tumor burden, local treatment procedures such as hepatectomy, RFA, or microwave ablation are employed. However, the efficacy of such treatments remains controversial.[14]

The effectiveness and stability of local treatment in managing liver metastasis in various other carcinomas, including ovarian and colon cancer, has previously been confirmed.[15,16] In pancreatic cancer, some studies have attempted local therapy for hepatic metastasis.[17,18] In 1982, Morrow, et al.[19] documented hepatectomy for liver metastases originating from pancreatic cancer. Since then, hepatectomy has been adopted and investigated in numerous centers for the treatment of liver metastases; however, its effectiveness remains controversial.[3,17] Historically, relying solely on surgical treatment for liver metastases from pancreatic cancer has not guaranteed long-term survival for many such patients. However, the recent emergence of CTx regimens, such as FOLFIRINOX, has led to more optimistic expectations for conversion surgery.[20-23] Omiya, et al.[24] proposed criteria for metastasectomy in pancreatic cancer,

Table 4. Multivariate Analysis of Variables in Relation to Patient OS

Variables	HR	Exp (B) (95% CI)	*p*-value
Early recurrence			
Within 6 months	18.485	4.933–69.262	<0.001
N stage			
N0	(Ref)		
N1	2.346	0.949–5.803	0.065
N2	0.410	0.044–3.790	0.432
Adjuvant regime			
Gemcitabine base	(Ref)		
Xeloda base	1.094	0.244–4.898	0.907
5-FU base	4.775	1.436–15.880	0.011
FOLFIRINOX base	3.248	0.672–15.697	0.143
CTx after liver metastasis regime			
Gemcitabine base	(Ref)		
Xeloda base	3.445	0.399–29.734	0.261
5-FU base	5.397	1.543–18.885	0.008
FOLFIRINOX base	0.580	0.215–1.565	0.282
Others	1.879	0.541–6.524	0.320

CI, confidence interval; CTx, chemotherapy; Exp(B) exponential of B; FU, fluorouracil; HR, hazard ratio; OS, overall survival; Ref, reference.

Table 5. Cox Proportional Hazards Regression for NT and LT Group

Outcomes	HR	Exp(B) (95% CI)	*p*-value
OS	0.846	0.397–1.804	0.665
PRS	0.932	0.437–1.985	0.855
OS (adjustment*)	0.387	0.143–1.049	0.062
PRS (adjustment)	0.469	0.181–1.211	0.118

CI, confidence interval; CTx, chemotherapy; Exp(B), exponential of B, HR, hazard ratio; OS, overall survival; PRS, post-recurrence survival.
*The adjustment variables were N stage, adjuvant CTx regimen, CTx after liver metastasis regime, and early recurrence rate (within 6 months).

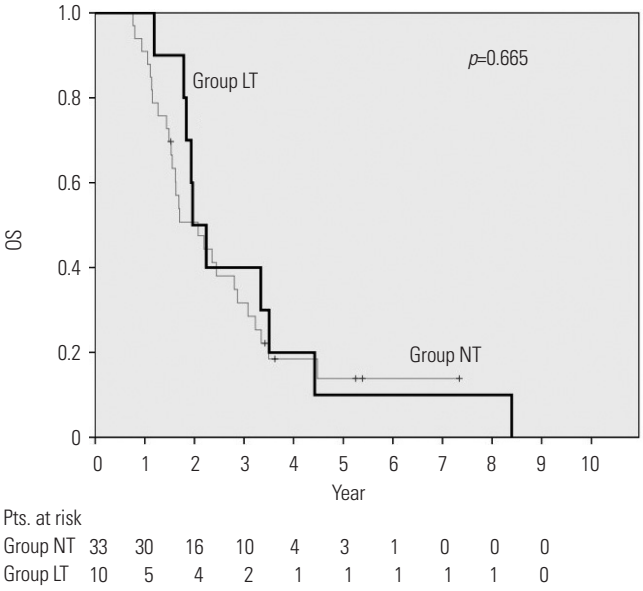

Fig. 2. Kaplan–Meier survival curve comparing OS between LT and NT groups. The survival difference was not statistically significant (p=0.665). OS, overall survival.

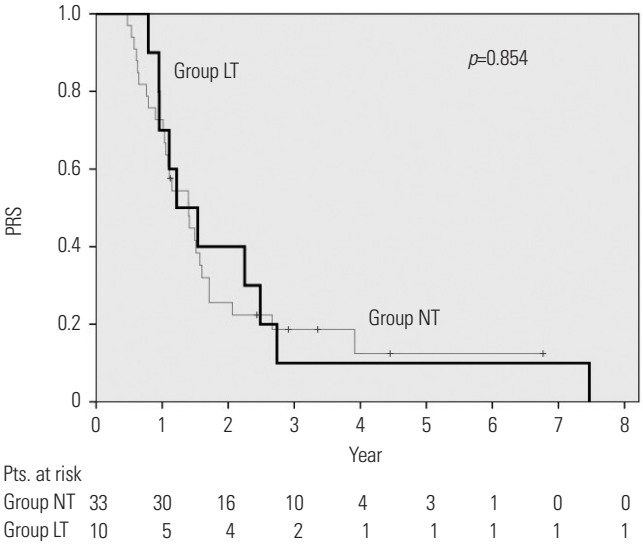

Fig. 3. Kaplan–Meier survival curve comparing PRS between LT and NT groups. The survival difference was not statistically significant (p=0.854). PRS, post-recurrence survival.

and Boag, et al.[25] defined oligometastasis and suggested treatment strategies. This advancement also applies to RFA, which offers minimally invasive and safety benefits.[13,14,18] Hua, et al.[18] reported that primary tumor location and the maximum diameter of the liver metastasis significantly affected the clinical efficacy of RFA in hepatic metastasis of pancreatic cancer. Lee, et al.[26] reported that patients with small-diameter tumors, early tumor, node, metastasis stage before curative surgery, late hepatic recurrence, and liver-only metastasis had better RFA-related outcomes.

In this study, using data from our institution, we aimed to investigate the oncologic role of administering local therapy to patients with PDAC who had undergone radical pancreatectomy and had liver metastases. We also investigated the factors that might influence survival outcomes in this patient group. No significant survival benefit was observed when local therapy was applied to liver oligometastases in the patients with PDAC who had received adjuvant CTx (Table 5). Therefore, it remains unclear whether local treatment is beneficial for such patients with liver metastases. To further investigate this aspect, the following two detailed case examples are presented (Table 1).

Patient No. 9 had a history of traumatic splenectomy 10 years prior to surgery. She underwent 2 months of gemcitabine-based neoadjuvant chemoradiation therapy (CCRT), followed by a DP and six cycles of adjuvant gemcitabine/erlotinib. On postoperative day 397, a 2.4-cm metastasis was detected in S4 of her liver. In response, RFA was performed, and the CTx regimen was switched to FOLFIRINOX. Following the RFA, thrombosis was observed near the left portal vein, and it was unclear whether this was a tumor thrombus or a benign thrombosis related to the RFA. However, the thrombosis resolved, and the

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RFA site remained stable with shunting in S4. This patient later experienced recurrence in the common bile duct and disease progression, but no recurrence or complications occurred at the S4 lesion, and she died on postoperative day 1218.

Patient No. 10 underwent a PPPD, followed by FOLFIRINOX and XELODA-based CCRT as adjuvant therapy. On postoperative day 383, a 2.1-cm liver metastasis was identified in S8. Despite subsequent treatment with five cycles of gemcitabine/abraxane, the liver lesion remained unchanged. Consequently, a right anterior sectionectomy was performed without postoperative complications. However, recurrence occurred at the hepatic hilum, and the patient died on postoperative day 671.

As observed in these two cases, local control of the liver lesions was successfully achieved without significant complications at the treated sites. In both patients, despite disease progression elsewhere, the locally treated metastases remained stable. This suggests that, for carefully selected patients such as those in good general condition and deemed to be surgically tolerable, and with a limited number of small lesions, local treatments such as RFA or resection may offer meaningful control of liver metastases. While our study findings did not show a clear survival benefit across the entire cohort, these individual cases highlight the potential of local therapy as a viable option for select patients with pancreatic cancer and liver oligometastasis.

The remarkable survival observed in Patient No. 9 may largely be attributed to the effect of the FOLFIRINOX regimen. As shown in Tables 3 and 4, there was a significant difference in survival outcomes based on the CTx regimen used. Specifically, as depicted in Table 3, patients who switched to a FOLFIRINOX-based regimen after liver metastasis showed a significantly lower HR, indicating improved survival prospects. These findings suggest that better outcomes could be anticipated with FOLFIRINOX-based therapies. Therefore, targeted follow-up studies focusing on local treatment, especially in patient groups likely to have a favorable prognosis, would be highly beneficial.[27-29]

This study had several limitations, including the potential for selection bias owing to its retrospective design. Pancreatic cancer specialists (gastroenterologists and hepatobiliary-pancreatic surgeons) at Severance Hospital considered local treatment for liver metastasis after pancreatic cancer surgery based on several criteria: a limited number of liver metastases, small lesion size, no further progression after CTx, and, in cases of simultaneous surgery, the primary tumor being resectable through standard procedures without the need for additional combined resections. Additionally, patients had to be in good general health. However, these criteria were not absolute, and treatment decisions were made subjectively, relying on the attending physician's judgment. Based on this approach, we retrospectively reviewed the cases using hospital data, ultimately including patients with an ASA PS score of ≤3 and those with ≤2 liver metastases. Despite this, significant differences were observed in BMI, ASA PS, tumor size, and T stage (Table 1), suggesting that physicians were more cautious in selecting patients for local treatment.

Another limitation was the small sample size of the study. An absence of standardized guidelines for local treatment during the study period made it challenging to collect a large number of cases. This limitation affected our ability to obtain statistically significant results. Future studies with larger datasets will be crucial in drawing more robust conclusions. Such studies will also be important in establishing clearer guidelines regarding the number and size of lesions that are most appropriate for localized treatment.

In conclusion, in this study, local treatments such as hepatectomy and RFA did not lead to significant improvements in OS or PRS for patients with PDAC who developed hepatic oligometastasis after curative pancreatectomy. However, case observations suggest that patients with fewer metastatic lesions or a favorable response to CTx may derive potential oncological benefits from a local treatment approach. These findings highlight the need for future studies with larger sample sizes to further investigate this potential.

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