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Liver resection for synchronous metastasis from adenocarcinoma of the pancreas: international multicenter cohort study

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Introduction: Treatment aiming to cure pancreatic ductal adenocarcinoma (PDAC) is primarily based on radical surgical resection. However, in most patients, distant metastases are already detectable at the time of diagnosis, preventing a curative treatment pathway.

Methods: Cases of PDAC with synchronous liver metastasis were collected from 14 international centers across multiple countries and continents. The study was promoted by the International Society of Liver Surgeons (ISLS) to define the role of simultaneous pancreatic and liver surgery in the treatment of oligometastatic PDAC. Overall survival (OS) and the cumulative incidence function of recurrence were estimated in a surgical cohort, and OS was compared with that of a non-surgical control group.

Results: Fifty patients were included in the surgical cohort. Most of the procedures were Whipples (60%), associated with wedge resections of the liver (86%). The median hospital stay was 10 days, with a median Comprehensive Complication Index (CCI) of 12, and 68% of the patients spent no more than 1 day in the intensive care unit (ICU). In the surgical group, OS at 6, 12, and 24 months after surgery was 83%, 69%, and 49%, respectively. The adjusted hazard ratio (HR) (surgical vs non-surgical cohort) was 0.26 (95% CI: 0.12–0.55, $P < 0.001$).

Conclusions: The results of this international multicenter study further support the hypothesis that oligometastatic PDAC represents an intermediate stage between localized and overtly metastatic cancer. Therefore, following primary chemotherapy and in carefully selected patients based on the A–B–C paradigm, resection of the primary pancreatic tumor along with liver metastases may be considered.

Keywords: distal pancreatectomy, hepatectomy, liver resection, MIPS, PDAC, RAMPS, Whipple

Introduction

Pancreatic ductal adenocarcinoma (PDAC) accounts for approximately 80% of all pancreatic malignancies[1], making it one of the most lethal cancers in the general population[2]. Surgical resection, combined with systemic chemotherapy, remains the only potentially curative treatment.

However, nearly 50% of patients present with metastatic disease at the time of diagnosis. Despite advances in both

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oncologic and surgical treatments, the management of metastatic PDAC continues to pose significant therapeutic challenges[3,4]. Due to hematogenous dissemination through the splenoportal–mesenteric axis, the liver is the most common site of metastasis[5,6].

The concept of oligometastatic disease was introduced to describe an intermediate stage between localized and widespread metastatic disease, which may be amenable to locoregional treatments[7]. Hepatic resection has been widely accepted as a potentially curative option for metastatic disease in various malignancies, such as colorectal cancer[8,9]. Additionally, surgical resection has demonstrated a survival benefit in patients with liver metastases from neuroendocrine tumors[10–12].

Recent evidence by Markar *et al* suggests that hepatic metastasectomy for gastric adenocarcinoma significantly improves overall survival (OS) (HR = 0.50; 95% CI: 0.41–0.61; $P < 0.001$). Furthermore, their findings indicate a greater survival benefit in patients with solitary hepatic metastases compared to those with multiple lesions (OR = 0.31; 95% CI: 0.13–0.76; $P = 0.011$)[13].

Historically, the role of hepatic resection in PDAC has been controversial. However, recent systematic reviews suggest that surgical resection of PDAC with synchronous liver-limited metastases may provide a survival benefit in select patients[14,15].

To further investigate this potential therapeutic strategy, we have designed a multicenter, international, retrospective study aimed at clarifying the role of liver resection in this patient cohort. The primary objective of this study is to evaluate the cumulative incidence function (CIF) of recurrence and OS following the surgical resection of synchronous liver-limited metastases from PDAC, compared to a control group of patients receiving only oncologic treatments.

HIGHLIGHTS

- Patients affected by pancreatic ductal adenocarcinoma with liver-limited oligometastatic disease may receive a surgical approach in very selected cases.
- Neoadjuvant chemotherapy represents a protective factor for survival, while CEA levels and tumor size are risk factors for shorter overall survival.
- After a favorable response to induction chemotherapy, resection significantly improves 1- and 3-year survival compared to chemotherapy alone.

Methods

Study design

This is a multicenter, retrospective study endorsed by the International Society of Liver Surgeons (ISLS). The study was approved by the local Ethical Committee. The study was conducted according to the STROCSS guidelines[16].

Clinical data, including patient demographics, operative details, chemotherapy regimens, and short- and long-term follow-up outcomes, were retrospectively collected from 14 high-volume hepatopancreatobiliary (HPB) centers. The study population comprises patients with a preoperative diagnosis of synchronous oligometastatic PDAC, the majority of whom underwent neoadjuvant chemotherapy. Surgery was considered a possible treatment option in patients with a positive response to primary/neoadjuvant chemotherapy (i.e., meeting the A–B–C paradigm, despite the presence of oligometastases).

Additionally, a subset of patients included in the surgical cohort had no preoperative diagnosis of oligometastatic disease but underwent upfront curative-intent pancreatic resection, with intraoperative detection of synchronous liver metastases. All liver metastases, whether diagnosed preoperatively or intraoperatively, were synchronous.

Pancreatic resections performed in this cohort included pancreatoduodenectomy, distal pancreatectomy, and total pancreatectomy. Hepatic resections were classified as either major or minor resections, based on the extent of liver involvement.

For comparison, patients who received standard-of-care systemic chemotherapy instead of surgery for resectable PDAC with known oligometastatic liver disease were selected as a control group.

Statistical methods

Continuous variables were reported as medians and interquartile ranges (IQRs). Categorical variables were reported as counts and percentages.

The OS function was estimated using the Kaplan–Meier method, and the log-rank test was used to assess differences between groups. The cumulative incidence function (CIF) of recurrence was estimated according to the method described by Kalbfleisch and Prentice[17], considering death as a competing event.

Univariable Cox proportional hazards regression models were used to assess the association between several factors and OS. Variables with $P < 0.10$ in the univariable analysis were included in the multivariable analysis.

Wilcoxon's signed-rank test for continuous variables and Fisher's exact test for categorical variables were used to compare the distribution of the evaluated characteristics between surgical and non-surgical patients.

A univariable Cox proportional hazards regression model was used to compare the OS between surgical and non-surgical patients. To adjust the estimated HR, variables that showed significant imbalance between the two groups (CA19-9, pancreatic tumor size, and pancreatic tumor location) were included in a multivariable Cox model.

All reported *P*-values were two-sided, with a *P*-value less than 0.05 considered statistically significant.

All statistical analyses were conducted using SAS software, version 9.4 (SAS Institute, Cary, NC, USA).

Results

A total of 90 patients diagnosed with PDAC with synchronous liver metastases were included in the study.

Surgical group characteristics

The surgical cohort ($n = 50$) had a median age of 68 years (IQR: 58–72), with a male predominance ($n = 27$, 54%). The median Charlson comorbidity index in this group was 8, ranging between 7 and 10 (IQR). At the time of surgery, the median bilirubin level was 9.1 μmol/L (IQR: 1.6–36), while the median

carcinoembryonic antigen (CEA) and carbohydrate antigen (CA) 19-9 levels were 5.0 ng/mL (IQR: 2.1–23) and 149 U/mL (IQR: 42–850), respectively.

Most primary tumors were located in the pancreatic head (n = 30, 60%). At diagnosis, the majority of tumors were considered resectable (n = 34, 68%), and 21 patients (42%) had no evidence of liver metastases. Notably, 86% of the cases were staged using a CT scan only. Vascular involvement was present in 14 patients, with invasion of the superior mesenteric vein (SMV) in 11 cases and the superior mesenteric artery (SMA) in 3 cases. The median pancreatic tumor size at diagnosis was 30 mm (IQR: 20–38), and the median total size of liver metastases was 14 mm (IQR: 9–24). Preoperative and oncological data at diagnosis in the surgical group are summarized in Table 1.

A total of 29 patients (58%) were diagnosed with oligometastatic PDAC during pre-operative staging, with one or more liver metastases, while the other cases were identified intraoperatively. Liver metastases were evenly distributed between the left and right hemi-livers, with single-segment involvement in the majority of cases. Neoadjuvant chemotherapy was received by 46% of the cases. Of the 23 patients who received neoadjuvant chemotherapy, 39% were treated with Gemcitabine-based regimens (4 received Gemcitabine-Abraxane, 1 Gemcitabine alone and 1 Gemcitabine-5-fluorouracil, 3 Gemcitabine-cisplatin), 48% received FOLFIRINOX (11 cases, including one that also received Gemcitabine and Paclitaxel), 4.3% (1 case) received FOLFIRI, and 8.7% (2 cases) received FOLFOX. Three out of 23 patients experienced a reduction in liver metastasis size following neoadjuvant chemotherapy (response), two showed an increase in liver metastasis size following neoadjuvant chemotherapy (progression), while liver metastasis size remained stable in 18 out of 23 patients after neoadjuvant chemotherapy (stable disease).

The most frequently performed pancreatic procedure was pancreatoduodenectomy using the Whipple technique (n = 30, 60%). Hepatic resection was predominantly performed as a wedge resection (n = 42, 86%). Additionally, vascular resection was required in nine patients (18%). One patient underwent a concomitant left adrenalectomy. Intraoperative transfusion of one or more units of packed red blood cells (pRBCs) was required in 32% of the cases.

Postoperative outcomes and pathological findings

Table 2 summarizes short-term outcomes and histological details. Following surgery, the median hospital stay was 10 days (IQR: 9–15), with a median Comprehensive Complication Index (CCI) of 12 (IQR: 8–21). The majority of patients (n = 34, 68%) spent no more than 1 day in the intensive care unit (ICU). There was no peri-operative mortality at 30 and 90 days.

Histopathological examination revealed that most primary tumors were either moderately differentiated (grade 2, n = 24, 48%) or poorly differentiated (grade 3, n = 15, 30%), with a median tumor size of 21 mm (IQR: 11–35). The median number of positive lymph nodes was 2 (IQR: 0–5), with a median of 16 lymph nodes retrieved (IQR: 11–26). Surgical margins were positive (R1) in six patients (13%).

Most patients had a single active liver metastasis (n = 32, 64%), with a median total size of 12 mm (IQR: 8–21). All metastases were resected with negative (R0) margins. Adjuvant chemotherapy was administered to 31 patients (62%), while three patients also received radiotherapy.

Control group characteristics and comparison

The control group accounted for 48 cases, eight of whom were excluded due to missing follow-up information. Forty cases of patients affected by resectable PDAC with synchronous oligometastatic liver disease were ultimately compared to the surgical cohort. The distribution of pancreatic lesions differed between groups, with both cohorts showing a predominance of tumors located in the pancreatic head. However, the control group had no cases of lesions in the pancreatic body or uncinate process. A detailed comparison of demographic and oncologic data between the two groups is presented in Table 3.

Survival and recurrence outcomes

In the surgical group, OS at 6, 12, and 24 months after surgery was 83% (95% CI: 68–91), 69% (95% CI: 53–81), and 49% (95% CI: 32–64), respectively (Fig. 1a). CEA level, tumor size, and administration of neoadjuvant chemotherapy were significantly associated with OS, with the latter demonstrating a protective effect (HR: 1.04, 1.13, and 0.40, respectively) (Table 4). Figure 2 shows a comparison of OS curves for resected patients who received neoadjuvant chemotherapy compared to those who underwent upfront surgery. During follow-up, 28 (56%) patients in the surgical group experienced disease recurrence. Of these, three patients had locoregional recurrence, while 25 developed distant metastases. Six patients experienced death as the first event and were considered competing events. The CIF was 23% (95% CI: 12–36) at 6 months, 46% (95% CI: 30–61) at 12 months, and 58% (95% CI: 40–72) at 24 months (Fig. 3).

In the non-surgical group, OS at 6, 12, and 24 months after diagnosis was 55% (95% CI: 39–69), 23% (95% CI: 11–36), and 13% (95% CI: 5–25), respectively (Fig. 1B and C).

The univariable HR comparing the surgical and non-surgical cohorts was 0.32 (95% CI: 0.19–0.53, $P < 0.001$). After adjusting for variables that showed a significant imbalance between the two groups (CA19-9, pancreatic tumor size, and pancreatic tumor location) in a multivariable model, the HR was 0.26 (95% CI: 0.12–0.55, $P < 0.001$).

Discussion

This study shows that patients presenting with oligometastatic PDAC may receive surgery as part of their treatment, with favorable short-term outcomes and good results in terms of OS. Patient selection is a crucial factor in determining the survival benefits of surgical intervention for oligometastatic PDAC[15,18,19]; and in this study, tumor size, CEA level, and neoadjuvant chemotherapy demonstrated a statistically significant correlation with OS.

Radiological staging plays a key role in assessing local tumor extension, metastatic organ involvement, and the number and size of lesions. Despite advancements in imaging technologies, approximately 8% of PDAC cases present with occult metastases[20]. Additionally, evaluating tumor response to neoadjuvant chemotherapy remains a critical step; however, a universally accepted definition of oligometastatic disease is still

Table 1

Demographic, disease and treatment characteristics of the surgical group (*N* = 50).

Variable	Level	Overall (*N* = 50)
Age (y), median (IQR)		68 (58–72)
Gender, *N* (%)	Male	27 (54)
	Female	23 (46)
BMI (kg/m^2), median (IQR)[d]		23.0 (20.0–26.3)
Charlson Comorbidity Index, median (IQR)[e]		8 (7–10)
Bilirubin (µmol/L), median (IQR)		9.1 (1.6–36.0)
CEA (µg/L), median (IQR)		5.0 (2.1–23.0)
CA19-9 (U/mL), median (IQR)		149 (42–850)
Pancreatic tumor size (mm), median (IQR)		30 (20–38)
Pancreatic tumor location, *N* (%)	Head	30 (60)
	Body	7 (14)
	Uncinate	4 (8)
	Neck	2 (4)
	Tail	7 (14)
ASA status, *N* (%)	ASA 1	5 (10)
	ASA 2	29 (58)
	ASA 3	16 (32)
Diagnostic methodology, *N* (%)	CT	43 (86)
	MRI	7 (14)
Staging at diagnosis, *N* (%)	Resectable	34 (68)
	Borderline Resectable	14 (28)
	Unresectable	2 (4)
Vascular infiltration, *N* (%)	No	36 (72)
	SMV	11 (22)
	SMA	3 (6)
Liver metastasis at diagnosis, *N* (%)	No	21 (42)
	Yes	29 (58)
Extrahepatic metastasis at diagnosis, *N* (%)	No	47 (94)
	Yes	3 (6)[c]
Total size of liver metastasis at diagnosis (mm), median (IQR)		14 (9-24)
Neoadjuvant chemotherapy, *N* (%)	No	27 (54)
	Yes[a,b]	23 (46)
Blood transfusion (units), *N* (%)	0	34 (68)
	≥1	16 (32)
Pancreatic procedure performed, *N* (%)	Pancreatoduodenectomy – Whipple's	30 (60)
	Distal pancreatectomy	11 (22)
	Pancreatoduodenectomy – pylorus preserving (PPPD)	2 (4)
	Total pancreatectomy	7 (14)
Spleen resection, *N* (%)	No	27 (54)
	Yes	23 (46)
Vascular resection, *N* (%)	No	41 (82)
	Yes	9 (18)
Type of liver resection, *N* (%)[f]	Wedge	42 (86)
	Segmentectomy	2 (4)
	Extended left	1 (2)
	Extended right	1 (2)
	Other	3 (6)

[a]Median total size of liver metastases after neoadjuvant chemotherapy: 16 mm (IQR: 11–25 mm)
[b]Three out of 23 patients experienced a reduction in liver metastasis size following neoadjuvant chemotherapy (Response), two out of 23 patients experienced an increase in liver metastasis size following neoadjuvant chemotherapy (No response),
[c]Two lungs, one bone
Liver metastasis size remained stable in 18 out of 23 patients after neoadjuvant chemotherapy (No response)
[d]Two missing
[e]Six missing
[f]One missing

lacking[21,22]. Studies vary significantly in their selection criteria for surgical candidates, particularly regarding liver metastases at diagnosis and their response to neoadjuvant treatment. Some studies have only considered resection after the complete disappearance of liver metastases or the presence of a single residual lesion following chemotherapy[23–25]. Others have allowed up to six metastatic lesions[26], while some have focused on a combination of lesion size and number, irrespective of chemotherapy response[27]. Future research may incorporate metabolic response assessments using FDG-PET imaging to refine patient selection[28]. In our study, all patients underwent simultaneous resection of liver metastases and the primary pancreatic tumor. Notably, nearly half of the cases did not receive neoadjuvant chemotherapy, primarily due to the intraoperative diagnosis of metastatic liver lesions. However, our findings indicate that neoadjuvant chemotherapy has a statistically significant correlation with OS, showing that those patients who did not receive it have an increased risk of shorter survival.

Another key factor in patient selection is tumor biology. Molecular markers, such as CA19-9, have been commonly used as inclusion criteria in previous studies[23–25], although no standardized cut-off values have been established. Takeda *et al* demonstrated that patients with oligometastatic PDAC had lower median CA19-9 levels than those with multi-organ metastases. Furthermore, patients with serum CA19-9 levels below 1000 U/mL exhibited improved OS[29]. CEA has also been proposed as a potential biomarker for predicting chemotherapy response in oligometastatic PDAC[30]. Additionally, liquid biopsy techniques, such as circulating tumor DNA (ctDNA) detection, have been linked to worse OS and a higher metastatic burden in advanced PDAC[31]. We herein provide evidence of a positive correlation between preoperative CEA levels and OS in patients who underwent concomitant pancreatic and liver surgery for oligometastatic PDAC, which may be helpful in selecting patients presenting with such a condition for surgical treatment. CA19-9 seems to be related to OS as well, although it did not reach a statistically significant threshold in the univariable analysis (HR + 100 U/mL = 1.02, 95% CI: 1.00–1.03, $P = 0.079$).

Recent advances in molecular profiling have enabled a more precise characterization of PDAC genomic alterations. Several

Table 2

Short-term outcomes, pancreas/liver histology and follow-up in the surgical group (*N* = 50).

Variable	Level	Overall (*N* = 50)
ICU stay (days), *N* (%)	0	15 (30)
	1	19 (38)
	2	8 (16)
	>2	8 (16)
In hospital stay (days), median (IQR)		10 (9–15)
Comprehensive Complication Index (CCI), median (IQR)		12 (8–21)
Pancreas histology		
Number of positive nodes, median (IQR)		2 (0–5)
Number of total nodes, median (IQR)		16 (11–26)
Size (mm), median (IQR)		21 (11–35)
Grade, *N* (%)	0	3 (6)
	1	7 (14)
	2	24 (48)
	3	15 (30)
	4	1 (2)
Margin (mm), median (IQR)		3.5 (1.0–10.0)
R status, *N* (%)[a]	R0	41 (87)
	R1	6 (13)
Liver histology		
Number of active metastasis, *N* (%)	0	8 (16)
	1	32 (64)
	2	6 (12)
	3	3 (6)
	5	1 (2)
Max size (mm), median (IQR)		12 (7–20)
Total size (mm), median (IQR)		12 (8–21)
Margin (mm), median (IQR)		5 (2–10)
R status, *N* (%)[b]	R0	48 (100)
Follow-up		
Adjuvant chemotherapy, *N* (%)	No	19 (38)
	Yes	31 (62)
Radiotherapy, *N* (%)	No	47 (94)
	Yes	3 (6)
Number of metastasis after adjuvant therapy, *N* (%)	No	39 (78)
	Yes	11 (22)

[a]Three missing.
[b]Two missing.

Table 3

Demographic and disease characteristics among surgical and non-surgical patients.

Variable	Level	Surgical patients (*N* = 50)	Non-surgical patients (*N* = 40)	*P*-Value
Age (y), median (IQR)		68 (58–72)	68 (60–74)[a]	0.70
Gender, *N* (%)	Male	27 (54)	22 (55)	1.00
	Female	23 (46)	18 (45)	
BMI (kg/m^2), median (IQR)		23.0 (20.0–26.3)[b]	21.0 (19.5–23.5)[c]	0.16
CEA (ug/L), median (IQR)		5.0 (2.1–23.0)	13.5 (4.5–29.0)[d]	0.24
CA19-9 (U/mL), median (IQR)		149 (42–850)	2070 (80–4701)[e]	**0.004**
Pancreatic tumor size (mm), median (IQR)		30 (20–38)	36 (33–46)	**< 0.001**
Pancreatic tumor location, *N* (%)	Head	30 (60)	20 (50)	**0.001**
	Body	7 (14)	0 (0)	
	Uncinate	4 (8)	0 (0)	
	Neck	2 (4)	9 (23)	
	Tail	7 (14)	11 (28)	

[a]One missing.
[b]Two missing.
[c]Twenty-four missing.
[d]Eleven missing.
[e]Ten missing.
Bold values are those statistically significant.

gene mutations, including BRCA1/2, ATM, and CDKN2A, are associated with an increased risk of developing PDAC[32]. Approximately 10% of PDAC cases harbor pathogenic germline mutations, which may render them susceptible to targeted therapies[33,34]. In light of these findings, the NCCN guidelines now recommend routine genetic testing for all newly diagnosed PDAC patients[35]. In the context of oligometastatic PDAC, the integration of targeted therapies with chemo-radiation in patients with known gene mutations may enhance the efficacy of liver resection by specifically addressing metastatic disease[36]. Multimodal treatment strategies, incorporating cytotoxic chemotherapy, radiotherapy, and immunomodulatory agents, have also shown promising outcomes in metastatic PDAC[37,38].

The treatment of oligometastatic PDAC is inherently multimodal, encompassing prolonged systemic chemotherapy, major surgery, and potential additional therapies such as radiation, targeted therapy, or immunomodulating agents. This complex treatment regimen imposes a significant physiological burden, necessitating careful assessment of patient performance status. Neoadjuvant chemotherapy in our study showed a significant correlation with OS. A retrospective study comparing oligometastatic PDAC patients treated with chemotherapy and simultaneous pancreatic-liver surgery to two matched cohorts – one receiving chemotherapy alone and another undergoing surgery for non-metastatic PDAC – identified Eastern Cooperative Oncology Group (ECOG) performance status as a key predictor of OS[37]. In this context, minimally invasive surgical approaches could play a role in reducing operative morbidity[39], particularly in frail patients[40,41]. Despite successful resection, the risk of recurrence remains high, reflecting the inherent aggressiveness of pancreatic cancer. The rapid reappearance of metastases underscores the importance of close postoperative surveillance and early intervention strategies. Beyond recurrence monitoring, optimizing patient selection through multiparametric evaluations is critical to maximize the benefits of surgical intervention while avoiding futile treatments. Nonetheless, this study highlighted a significantly higher survival in the surgical group, with an adjusted HR of 0.26 ($P < 0.001$). This study has several limitations, including its retrospective nature, potential selection bias, and the small number of cases included. However, the results highlighted are consistent with the natural history of the disease and the well-known impact of pancreatic surgery in frail patients. Postoperative results are encouraging, with a low incidence of complications, short ICU and in-hospital stays, and appropriate oncological staging despite the two-site resections. Therefore, young patients with low comorbidity requiring a limited liver resection along with pancreatoduodenectomy or distal pancreatectomy should be carefully evaluated for a potential surgical approach. The development of advanced tools for

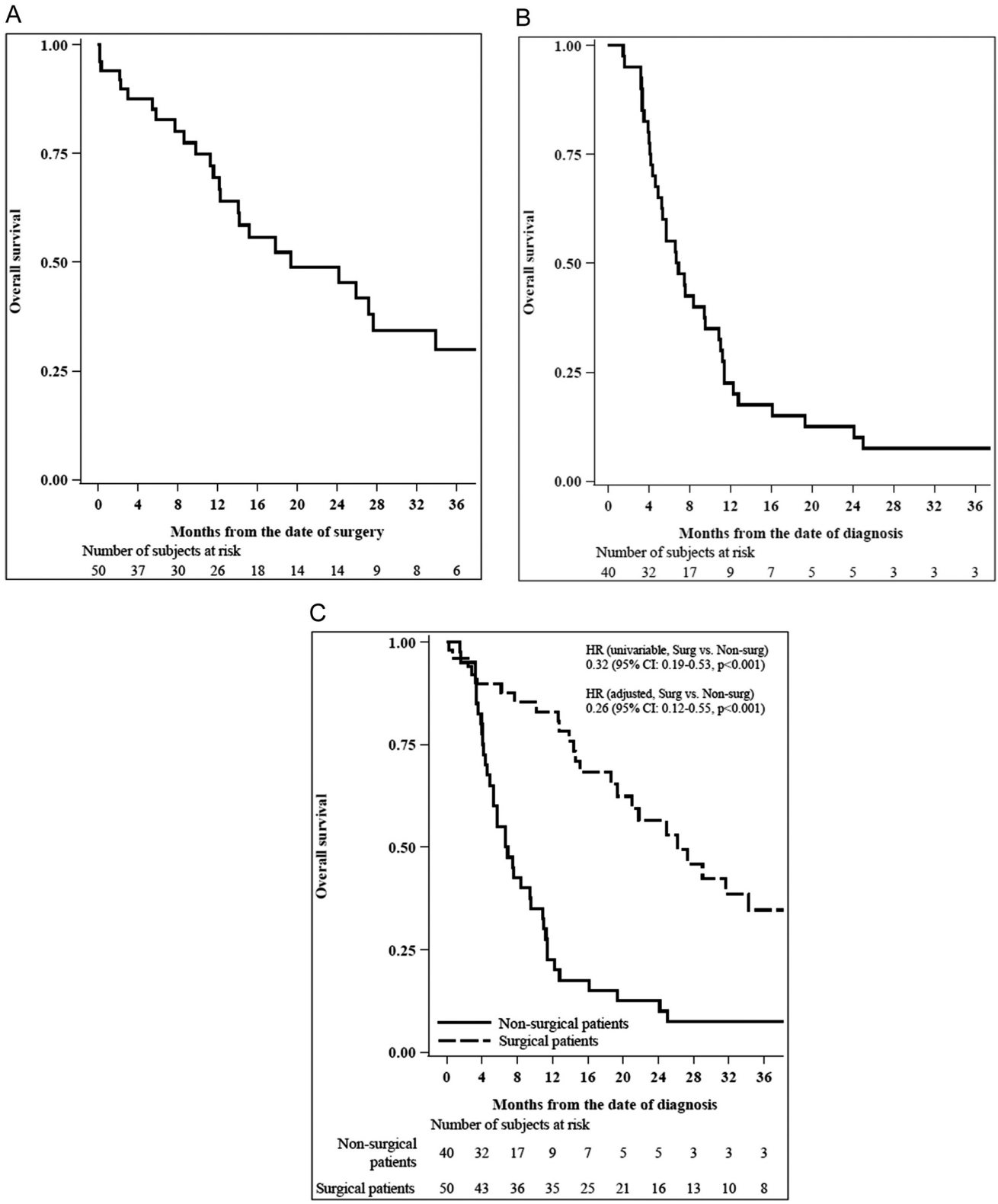

Figure 1. Overall survival (A) in the surgical group [*N* = 50, median FU (IQR) in months: 12 (3–26)]; (B) in the non-surgical group [*N* = 40, median FU (IQR) in months: 7 (4–11)]; (C) among surgical and non-surgical patients.

Table 4

Association of demographic, disease and treatment characteristics with overall survival in the surgical group (*N* = 50).

			Univariable analysis			Multivariable analysis		
Variable	**Level**	***N***	**HR**	**95% CI**	***P*-Value**	**HR**	**95% CI**	***P*-Value**
Age	+5 years		1.07	0.90–1.28	0.42			
Gender	Male	27	Ref.	-	-			
	Female	23	1.08	0.51–2.28	0.83			
BMI	+1 kg/m^2		1.02	0.92–1.13	0.68			
Charlson Comorbidity Index	+1		1.05	0.91–1.21	0.53			
Bilirubin	+10 µmol/L		1.00	0.99–1.01	0.80			
CEA	+10 ug/L		1.04	1.00–1.07	**0.041**	1.03	1.00–1.07	0.085
CA19-9	+100 U/mL		1.02	1.00–1.03	0.079	1.02	1.00–1.04	**0.019**
Pancreatic tumor size	+5 mm		1.13	1.01–1.26	**0.030**	1.14	1.02–1.27	**0.025**
Pancreatic tumor location	Head	30	Ref.	-	-			
	Other	20	0.72	0.32–1.60	0.42			
ASA status	ASA 1-2	34	Ref.	-	-			
	ASA 3	16	1.04	0.47–2.31	0.92			
Staging at diagnosis	Resectable	34	Ref.	-	-			
	Borderline Resectable/Unresectable	16	1.81	0.82–3.98	0.14			
Vascular infiltration	No	36	Ref.	-	-			
	SMV/SMA	14	1.69	0.75–3.81	0.21			
Liver metastasis at diagnosis	No	21	Ref.	-	-			
	Yes	29	1.03	0.48–2.18	0.94			
Total size of liver metastasis at diagnosis	+5 mm		1.06	0.94–1.20	0.36			
Neoadjuvant chemotherapy	No	27	Ref.	-	-	Ref.	-	-
	Yes	23	0.40	0.17–0.94	**0.037**	0.36	0.15–0.86	**0.022**

Bold values are those statistically significant.

identifying optimal surgical candidates is highly desirable. In the future, machine-learning algorithms may support clinicians in tailoring treatment strategies to individual patients, ensuring that they receive therapies most likely to yield favorable outcomes.

Conclusions

Our study suggests a potential role for surgical resection in patients with synchronous, liver-limited metastatic PDAC,

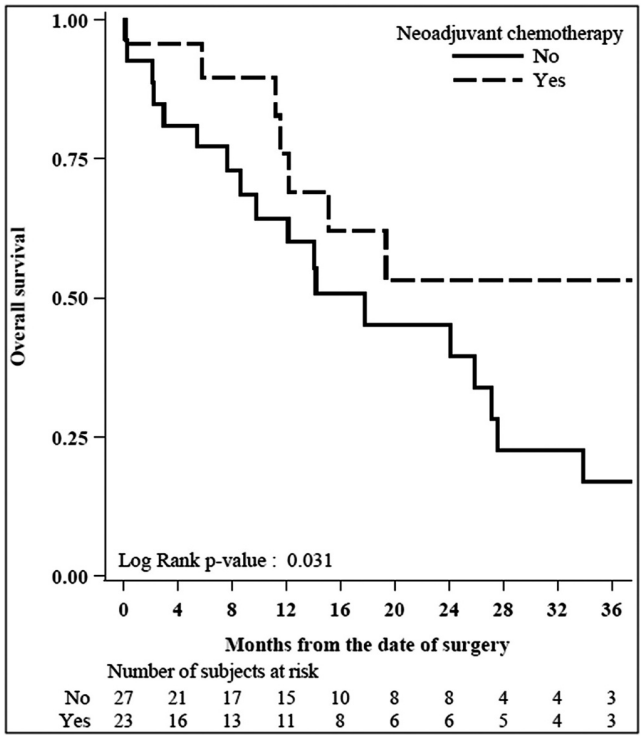

Figure 2. Overall survival among surgical patients stratified by neoadjuvant chemotherapy.

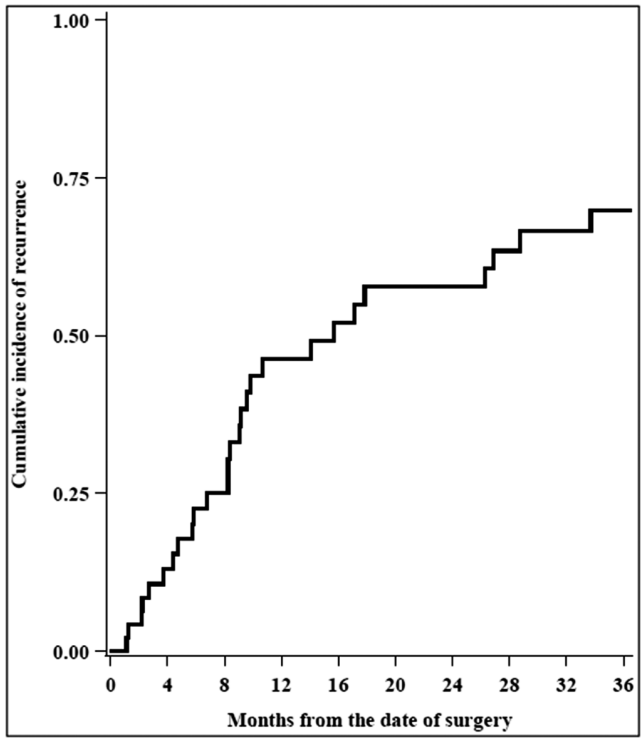

Figure 3. Cumulative incidence of recurrence in the surgical group (*N* = 50).

highlighting the importance of careful patient selection to achieve favorable OS and recurrence-free survival outcomes. Further integration of molecular and genetic analyses may help identify those who would derive the greatest benefit from an aggressive surgical approach.

Ethical approval

The study was approved by the AVEN (Area Vasta Nord, Italy) Ethics Committee (396/2021/OSS/AOUMO SIRER ID 2541).

Consent

None.

Sources of funding

None.

Author contributions

P.M.: study concept and design, data collection, data interpretation, writing the paper; C.G.: data collection, data interpretation, writing the paper; A.S. and K.V.: data collection, data interpretation, validation; S.F.: statistical analysis, validation; V.B.: statistical analysis, validation; A.B.: data collection, data interpretation, and validation; R.K., N.M., K.O., A.S., and A.Y. G.: data collection, data interpretation, validation; M.V.: data collection, data interpretation, and validation; R.M., E.K., F.R., and R.H.B.: data collection, data interpretation, validation; U.B. and L.D.C.: data collection, data interpretation, and validation; N.K. and S.D.S.: data collection, data interpretation, validation; M.D.: data collection, data interpretation, and validation; D.B.: data collection, data interpretation, validation; O.J.T.: study concept and design, critical revision; F.D.B.: study concept and design, manuscript editing, and critical revision.

Conflicts of interest disclosure

Andrea Spallanzani: Consultant and Advisory board: MSD, Astellas, AstraZeneca, Daiichi. All others: none.

Guarantor

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