Patterns of Recurrence After Curative Resection for Pancreatic Adenocarcinoma: A Single Institution Experience

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Introduction

- Pancreatic adenocarcinoma (PDAC) is one of the leading causes of death in developed countries and prognosis remains poor, in contrast to other types of cancer
- Only a small proportion of patients with resectable disease are eligible for surgery
- Rates of recurrence up to 92% and median overall survival between 1-3 years have been reported after curative surgery[1]
- How pancreatic cancer recurs in patients and why it does so is poorly understood with no unifying consensus
- There is no clear consensus on how to follow-up pancreatic cancer patients after curative resection in the UK
- A better understanding of how PDAC recurs after curative surgery could help influence and tailor specific follow-up regimens
- This study will focus on how various factors affect patterns and locations of first site PDAC recurrence after curative surgery

Aims

The aims of this study was to investigate patterns and factors affecting recurrence after curative resection of PDAC.

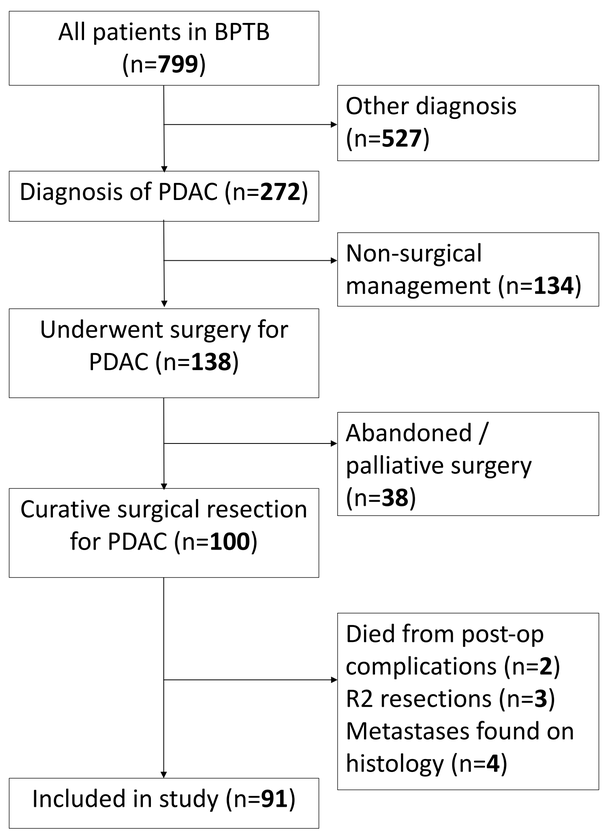
Methods

All consented patients from the prospectively maintained Barts Pancreatic Tissue Bank (BPTB) were screened for study inclusion.

Follow-up was either with an oncologist or 6-monthly CT scans + Ca19-9 blood tests with a HPB surgeon for at least 5 years. Recurrence detection was based on CT scan results.

X-tile Software[2] was used to identify optimal cut-off values for continuous variables and SPSS version 28 was used for all other analysis. Survival and recurrence analysis were undertaken using Cox proportional hazards model with a cut-off *p*-value of 0.05. Significant univariate co-variates were included into multivariate analysis subject to having <10% missing values and a test for multicollinearity with a variance inflation factor <5.[3]

Figure 1. Flow chart of patient enrolment



Results

- 91 patients consisting of 42 (46%) males and median age of 70.7 (range 43-86) years underwent curative surgical resection for PDAC between 2011 and 2022
- Median follow-up was 50.7 months (95% CI 40.3 – 61 months)
- 59 (65%) patients had PDAC in the head of the pancreas, 16 (18%) in the tail, 4 (4%) in the body, 3 (3%) in the uncinate, 7 (8%) in >1 location and 2 (2%) with insufficient data
- Neo-adjuvant chemotherapy was given in 9 (10%) patients. Only 1 had Gemcitabine + Capecitabine while the rest had Folfirinox
- Adjuvant chemotherapy was given in 56 (62%) patients. 17 (19%) had Folfirinox and 38 (42%) had Gemcitabine +/- Capecitabine. 1 (1%) had insufficient data
- Recurrence was observed in 66 (72.5%) patients and stratification by recurrence location revealed no significant difference in DFS (*p*=0.241)
- Positive resection margin (R1) was significantly associated with locoregional recurrence (HR 2.1; 95%CI 1.1-4.1; *p*=0.03)

Table 1. Recurrence location statistics

Recurrence location	Location specific only	Total recurrence
Locoregional	12	41
Liver	11	32
Lung	5	20
Peritoneal	3	14
Simultaneous locoregional + distant metastatic	29	29
Multiple distant metastases	6	14

Figure 2. Time to recurrence (location specific only)

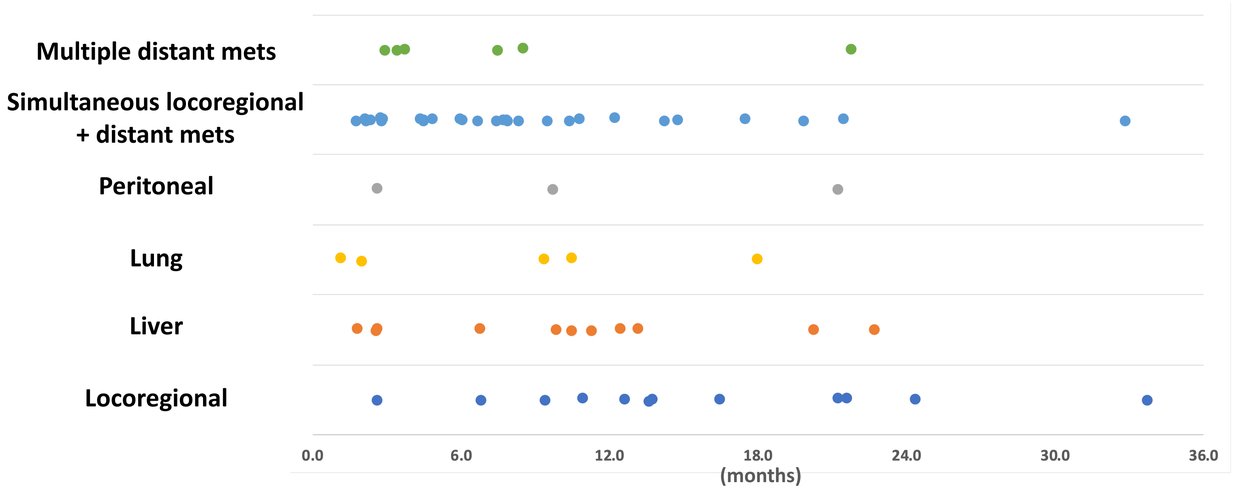
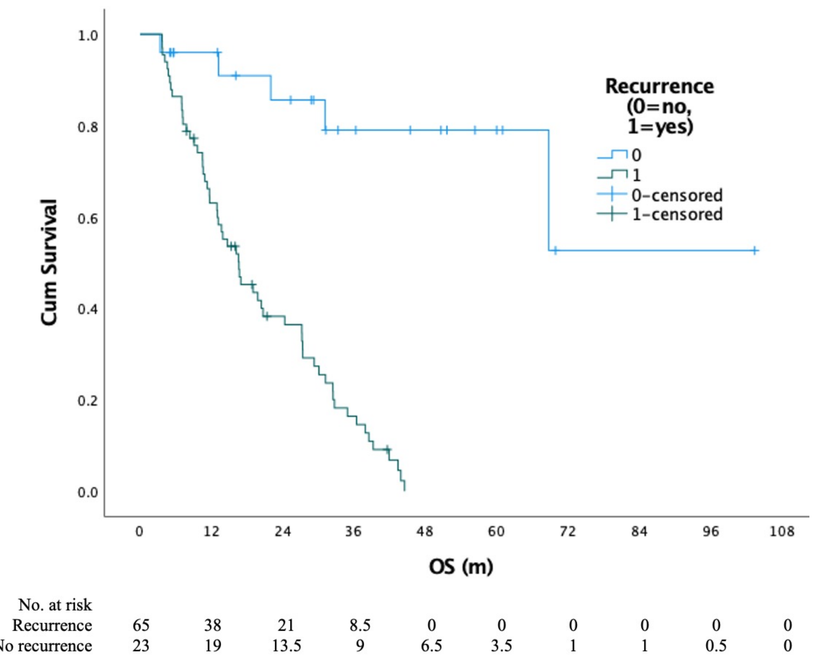


Figure 3. Kaplan Meier survival curve for recurrence vs no recurrence



- The recurrence group had a 1 and 2-year overall survival rate of 63% and 38% respectively
- The non-recurrence group had a 1 and 2-year overall survival rate of 98% and 86% respectively

Table 2. Significant predictors of survival and disease-free survival

Variable	*n*	Overall Survival				Disease-Free Survival			
		Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
		p value	HR (95% CI)	*p* value	HR (95% CI)	*p* value	HR (95% CI)	*p* value	HR (95% CI)
N stage		**<0.001**		**0.002**		**<0.001**		0.08	
0	26		1		1		1		1
1	46		3.6 (1.8-7.3)		0.5 (0.2-1.5)		3.3 (1.7-6.4)		3.1 (1.1-8.6)
2	19		7.7 (3.3-17.9)		2.1 (0.6-7.5)		4.9 (2.2-10.6)		2.3 (0.7-7.1)
Lymph node ratio		**<0.001**		**0.026**					
<0.12	34		1		1				
≥0.12	55		5.4 (2.9-10.2)		3.7 (1.2-11.4)				
Lymph node ratio						**<0.001**		**0.005**	
<0.33	62						1		1
≥0.33	27						4.7 (2.6-8.3)		2.8 (0.4-5.8)
Adjuvant chemotherapy		**0.002**		**0.01**		**0.004**		**0.002**	
None	34		1		1		1		1
Yes	56		0.5 (0.3-0.8)		0.4 (0.2-0.8)		0.5 (0.3-0.8)		0.4 (0.2-0.7)
Recurrence		**<0.001**		**<0.001**					
None	25		1		1				
Yes	66		11.7 (4.1-33.3)		36.8 (6-224.6)				
Systemic inflammation index		**0.01**		**0.007**					
<350	11		1		1				
≥350	77		3.4 (1.3-8.6)		11.4 (2-66.1)				
Systemic inflammation index						**0.011**		**0.01**	
<500	21						1		1
≥500	67						2.3 (1.2-4.3)		4.5 (1.4-14.3)
Pain		**0.012**		**<0.001**		0.099			
No	53		1		1		1		
Yes	38		1.9 (1.1-3.1)		3.6 (1.8-7.2)		1.5 (0.9-2.4)		

Discussion

- Time to recurrence did not differ significantly across recurrence locations possibly due to the small population size or limitations in detection (modality and follow-up regimens)
- Studies have highlighted limitations in detection of micrometastases and patient selection as reasons for early recurrence rates (63% <12mths) [4,5]
- Resection margin status was significantly predictive of locoregional recurrence but did not affect overall survival or overall recurrence in multivariate analysis
- 57% (n=20) of patients with R0 resections still had recurrence suggesting PDAC is a systemic disease at time of diagnosis[6]

Conclusion

There were no significant differences in timing to recurrence for different locations. More research is needed to investigate predictive factors for PDAC recurrence after curative resection in large national cohorts.

References

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