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Original Article

Outcomes after pancreatic resections for secondary tumors in the pancreas: a single-center experience

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ABSTRACT

Background: Isolated extrapancreatic metastatic disease within the pancreas is uncommon. This study aimed to examine the indications and outcomes of pancreatic resection for metastatic disease in non-pancreatic, nonneuroendocrine malignancy at a high-volume center.

Methods: This was a retrospective analysis of a prospectively managed database of pancreatic resections for metastatic disease for primary nonpancreatic, nonneuroendocrine tumors at the University Hospital Southampton. The collected and analyzed data included patient demographics, operative and perioperative outcomes, survival, and recurrence.

Results: A total of 844 patients who underwent pancreatic resection were examined. Of note, 26 consecutive patients met the inclusion criteria, representing 3.3% of the unit's throughput. The median disease-free interval was 65 months. Most resections were performed for renal cell carcinoma, followed by melanoma, breast cancer, and colorectal cancer. The perioperative morbidity was 42.9%, with 12 cases of post-operative complications. There were no perioperative deaths. The median overall survival was 41 months, whereas the median disease-free survival was 17 months for the entire cohort.

Conclusion: When coupled with the low morbidity and mortality rates of a high-volume pancreatic surgery center using careful patient selection, pancreatic metastectomy has the potential to result in good long-term survival.

Introduction

Isolated pancreatic metastases from extrapancreatic primary tumors are rare and constitute < 2% of all pancreatic malignancies [1]. The most common primary tumor to metastasize to the pancreas is renal cell carcinoma (RCC), with fewer reported cases from lung cancer, gastric cancer, colorectal cancer (CRC), melanoma, and breast cancer [2–5].

In the past 20 years, a concept of oligometastatic disease has emerged, in which these diseases are "limited in number and in location and are amenable to regional or curative treatment" despite the evidence of distant metastases [6,7]. For example, resections for colorectal, neuroendocrine, and other liver metastases have been shown to improve patient survival with low morbidity and mortality [8–10]. In addition, pulmonary resections for metastases from colorectal and other cancers have similar outcomes [11,12]. However, the evidence of resection for oligometastatic disease in the pancreas is currently limited. This is partly due to the low incidence of resectable solitary metastasis to the organ and due to the associated potential perioperative risks with pancreatic resections [13,14]. However, several high-volume centers have reported taking a

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considered approach to resecting patients with limited disease with a favorable tumor type and significant disease-free interval. Apart from RCC metastases, the potential risks and benefits of this approach remain poorly quantified [1,15,16].

This study aimed to examine the indications and outcomes of pancreatic resection for metastatic disease in a nonpancreatic, nonneuroendocrine malignancy at a high-volume pancreatic surgery center in the United Kingdom over the past decade.

Methods

This study was a retrospective analysis of a prospectively managed database of pancreatic resections at the University Hospital Southampton (UHS) between January 2010 and December 2024. The project was registered and approved with the hospital clinical governance department (project identification number: 7277), with data collection performed in line with the local audit policy, ensuring that appropriately pseudo-anonymized data were used for the analysis.

Patients who underwent resection for metastatic disease or primary extrapancreatic, nonneuroendocrine tumors were selected. Each patient was treated with curative intent, and the decision to proceed with surgery was made by the local multidisciplinary team. Patients with extrapancreatic metastases were included in which the extrapancreatic disease was deemed resectable. Patients with primary tumors that infiltrated the pancreas through local invasion were excluded.

Collected data included patient demographics, primary tumor pathology, disease-free interval, operation performed, extrapancreatic involvement, subsequent survival, and mode of recurrence. Collected perioperative outcomes included operative time, blood loss, postoperative complications, length of stay, number of tumors, and resection margin.

Operative morbidity was recorded according to the Clavien-Dindo classification [17]. It is our routine practice at UHS to place 1 abdominal drain lying next to the pancreatic resection margin in left pancreatectomy and 2 abdominal drains in pancreaticoduodenectomies (PDs). Pancreatic surgery–specific complications, such as pancreatic fistula, delayed gastric emptying, or postoperative hemorrhage, were determined as defined by the International Study Group for Pancreatic Surgery [18–20]. Postoperative bile leak was classified using the International Study Group of Liver Surgery definition [21]. Perioperative deaths were defined as death of any cause within 90 postoperative days. Grouped data were presented as median (IQR), unless otherwise specified. Disease-free interval was defined from the date of diagnosis of the primary tumor to the date of detection of metastasis to the pancreas. Overall survival (OS) was defined from the date of surgery to the date of death or the last date of follow-up, and recurrence-free survival was defined from the date of surgery to the date of recurrence or the last day of follow-up. Length of follow-up was defined from the date of diagnosis of the primary tumor to the last date of follow-up or the date of death. All data were correct up to May 20, 2025. All survival analyses were performed using the Kaplan-Meier method, and the differences in survival were compared using a log-rank method. A P value of $< .05$ was considered significant. All statistical analyses were performed using IBM SPSS Statistics for Windows (version 28; IBM), and mortality charts were generated using GraphPad Prism (version 8.4; GraphPad Software).

Results

During the studied period, the unit performed 844 pancreatic resections, most commonly for pancreatic adenocarcinoma or neuroendocrine tumors. Of note, 26 consecutive patients met the inclusion criteria of this study, representing 3.3% of the unit's throughput.

Table 1
Demographics table for all patients (N = 26).

Variable	n (%) or median (IQR)	Median DFI in months (IQR)
Male	16 (61.5)	–
Female	10 (38.5)	–
Median age at diagnosis of the primary tumor, y	54.5 (43.0–76.0)	–
Median age at pancreatic surgery, y	65.5 (46.0–80.0)	–
Overall median DFI, mo	65 (0–254)	–
Sites of the primary tumor		
Renal cell carcinoma	18 (69.2)	80 (8–254)
Malignant melanoma	3 (11.5)	14 (10–37)
Breast carcinoma	2 (7.7)	149 (65–232)
Sarcoma	1 (3.8)	15
Pulmonary adenocarcinoma	1 (3.8)	17
Rectal adenocarcinoma	1 (3.8)	40

DFI, disease-free interval.

The basic demographics are presented in Table 1. Of note, 16 of 26 patients (61.5%) were male, and the median age at the time of pancreatic surgery was 65 years. RCC was the most common site of primary tumor, representing 69.2% of the cohort, followed by malignant melanoma (11.5%) and breast carcinoma (7.7%). Among the 20 operative cases of RCC diagnosis, 11 (55%) had clear cell histology, 1 was papillary, and the remaining cases were unknown. Most patients presented with isolated pancreatic metastases. However, 2 patients (7.7%) with RCC presented with liver metastases in addition to pancreatic lesions, 1 patient with CRC presented with supraclavicular lymph node metastasis, and another patient with RCC origin presented with lung metastasis. There were 11 patients (42.3%) who had at least 1 extrapancreatic lesion before the detection of a metastatic lesion in the pancreas. Only 5 patients (19.2%) received adjuvant therapy after resection of their primary tumor. Of note, 1 patient with breast cancer completed a course of adjuvant tamoxifen, and another patient with breast cancer received adjuvant chemoradiotherapy. The patient with rectal cancer completed a course of adjuvant chemotherapy with panitumumab, and a patient with malignant melanoma received immunotherapy. Of note, 1 patient with metastatic RCC was receiving tyrosine kinase inhibitor (TKI) therapy before the diagnosis of a pancreatic metastasis, and another 3 patients were started on TKI treatment after diagnosis but before surgery.

Most patients (73.1%) proceeded to pancreatic surgery based on clinical suspicion from a previous history and radiological findings. Of note, 4 patients (15%) had a positive tissue diagnosis before pancreatic resection, with another 3 patients having negative cytology (11.5%) from endoscopic ultrasound–guided fine-needle aspiration.

The median disease-free interval was 65 months (IQR, 0–254). The longest interval between the diagnosis of a primary tumor and the detection of pancreatic metastasis was found with left RCC at 21.2 years, which was incidentally detected. Approximately 88.5% of the patients had metastases that were detected on surveillance imaging. Symptomatic presentations were seen in 3 patients: 1 patient with breast cancer presented with biliary obstruction, 1 patient with RCC presented with duodenal hemorrhage, and 1 patient presented with chest pain from RCC metastasis.

The location and distribution of the metastatic lesions in the pancreas are presented in Figs. 1 and 2. The metastases were most commonly found in the body and/or tail (n = 15 [57.7%]), followed by the head and/or neck and multiple sites in the pancreas. Of note, 7 patients (26.9%) had multiple lesions. However, 4 patients (15.3%) had multiple lesions in more than 1 region in the pancreas.

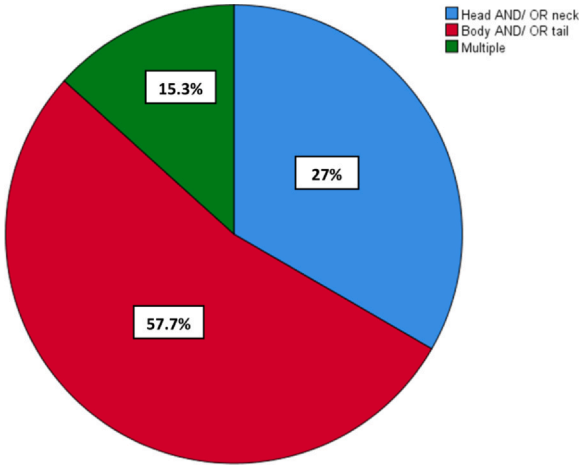

Figure 1. Site/location of the metastatic lesion in the pancreas.

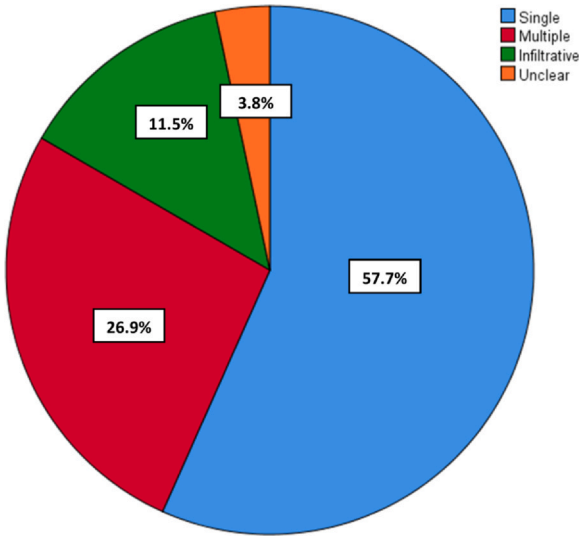

Figure 2. Distribution of the metastatic lesions in the pancreas.

The operative information and outcomes are presented in Table 2. There were 4 patients with RCC who presented with pancreatic metastasis twice, and 2 of the patients had 2 resections (both patients had a distal pancreatectomy and splenectomy performed initially, before having partial excision of the pancreas and pylorus-preserving completion total pancreatectomy at later dates). Therefore, each operative episode was analyzed separately (the total number of cases was 28). Approximately half of the patients (53.6%) had left pancreatectomy with or without splenectomy. In addition, 1 patient with RCC had additional enucleation from the head of the pancreas at the time of distal pancreatectomy for additional RCC metastases. Of note, 3 patients had additional visceral resection at the time of left pancreatectomy, which included wedge resection of the liver for RCC, left adrenalectomy for breast cancer metastasis, and neck dissection for CRC metastasis. Portal vein resections were performed in 2 patients from the overall cohort, incidentally for patients undergoing multivisceral resections for breast and CRC metastases mentioned above. A total of 8 patients (28.6%) had PD, of which 1 patient had pylorus-preserving pancreatectomy. Total pancreatectomy was performed in 4 patients (14.2%), all of whom had metastatic RCC. Among the 28 operations, there were 7 (25.0%) that involved laparoscopy, which were all for distal pancreatectomy and splenectomy. There were 2 robotic operations that were both for distal pancreatectomy and splenectomy. However, 1 operation was converted to open surgery during the operation.

Table 2
Intraoperative and postoperative data.

Operative information	Total (N = 28)[a]
Left pancreatectomy ± splenectomy	15 (53.6)
Pancreaticoduodenectomy	8 (28.6)
Total pancreatectomy	3 (10.7)
Partial excision of pancreas	1 (3.6)
Completion total pancreatectomy	1 (3.6)
Median operative time, min	300 (135–570)
Median blood loss, mL	500 (20–3500)
Median length of stay, d	7 (3–22)
Postoperative complications	
Pancreatic fistula	3 (10.7)
Bleeding/hematoma	3 (10.7)
Peripancreatic collections	2 (7.1)
Bile leak	2 (7.1)
Chyle leak	1 (3.6)
Infection	1 (3.6)
Chest drain insertion	1 (3.6)
Delayed gastric emptying requiring TPN	3 (10.7)
90-d mortality	0 (0.0)

TPN, total parenteral nutrition.
Data are presented as number (percentage) or median (IQR).
[a] Of note, 2 patients had 2 pancreatic resections for recurrence.

The median operative time was 300 min (IQR, 135–570), with a median blood loss of 500 mL (IQR, 20–3500). The median length of stay was 7 days (IQR, 3–22). The R1 resection rate was 21.4% (6/28) and occurred in 5 patients with RCC (1 patient with an enucleated RCC) and 1 patient who underwent multivisceral resection for CRC metastasis. Overall, postoperative complications were seen in 12 cases (42.8%). Of note, 1 patient underwent a same-day postoperative relook laparotomy for bleeding and was administered 12 units of blood perioperatively.

The median length of follow-up was 111 months (IQR, 50–301) from the diagnosis of the original primary tumor. Of the patients who underwent pancreatic resection, 15 of 26 (57.7%) were alive at the time of writing. The median OS for the entire cohort was 41 months, and the 3-, 5-, and 10-year survival rates were 76.9%, 65.3%, and 34.6%, respectively. The median OS of 18 patients with RCC was 35 months and was compared with the median OS of patients without RCC (72 months), although the difference was not statistically significant (P =.51).

Disease recurrences were observed in 60.7% of patients after pancreatectomies, with a median disease-free survival (DFS) of 17 months. The time to disease recurrence after pancreatectomy ranged from 1 to 127 months. The median DFS of patients without RCC was 39.5 months compared with 13.5 months in patients with RCC. However, the difference was not statistically significant (P =.36).

Discussion

Surgical intervention for synchronous and metachronous metastatic disease continues to evolve and has been proven to improve both survival and quality of life in select patients with favorable tumor pathology [22]. However, patients with metastases limited to the pancreas are relatively rare, and although there are some evidence to support pancreatic resection, with associated high morbidity and mortality associated with surgery, the benefit on oncological outcome remains limited. This paper aimed to add to the available evidence supporting resection in carefully selected patients.

Most pancreatic metastases are found during post-treatment surveillance imaging of the primary tumor. The utility of resection depends on the etiology and biology of an isolated pancreatic mass. All patients whose results were described in this study had their

history and imaging findings discussed at a multidisciplinary meeting before pancreatic resection. A history of a previous malignancy and features of the lesion on contrast-enhanced computed tomography (CT) guided the decision-making process. RCC commonly appears on CT as solitary or multiple nodules with homogeneous attenuation and distinct margins. Non-RCC metastases often have heterogeneous attenuation and an indistinct margin [23]. However, confirming the diagnosis of secondary pancreatic tumors on CTs while excluding other differential diagnoses of a primary pancreatic or neuroendocrine tumor can be difficult [24]. The multidisciplinary team requires as much information as possible to guide decision-making.

The signs and symptoms of isolated pancreatic metastases are often nonspecific or absent. Only 3 patients (10.7%) in our cohort had symptoms. The etiology behind their presentation was not known in 2 of the patients until after resection. Pathological examination of surgical specimens revealed breast cancer in one patient and RCC in another patient.

RCC made up the highest proportion of our patient cohort, which is similar to the experience of other major pancreatic surgery centers [1,16]. Because of the relatively high incidence of metastatic disease from RCC to the pancreas, most evidence around pancreatic metastectomy are reported with respect to this tumor type. The European Society for Medical Oncology Guidelines for RCC recommend selecting metastectomy while recognizing that there is a survival benefit that is difficult to quantify without bias [25]. After resection of solitary metastases to the pancreas, 5-year survival rates have been reported at 54% to 90%, a significantly higher survival rate than that for nonsurgical treatments of stage IV RCC and similar to the outcomes seen in our surgical cohort [1,15,16,26].

RCC metastases to the pancreas are commonly multiple, and it is important to be sure of the extent of the disease. It is our practice to perform intraoperative ultrasound to determine the resection margin and identify any additional disease. However, parenchymal preservation is key to preventing diabetes mellitus, which is particularly important as cytotoxic chemotherapy may be indicated in the setting of future disease progression. Total pancreatectomy is associated with morbidity and reduced quality of life and should be avoided when possible [16,27]. Formal resection may be of benefit in that it includes the removal of peripancreatic lymph nodes. However, there is no consensus that lymphadenectomy improves survival or recurrence rates [15,28].

Metastatic melanoma has a poor prognosis, and systemic therapies provide limited survival benefit. Isolated metastases to the pancreas are rare, and resection has been reported previously to result in a survival of 14 to 24 months [29]. The median survival of the 3 patients included in this study was 84 months. Our good survival result could be due to both patient selection and the significant improvements in systemic treatments for melanoma seen in recent years [30].

The morbidity and mortality of pancreatic resection have become significantly less over recent decades, and perioperative outcomes for resection of pancreatic metastases have not been shown to differ from those of pancreatic or neuroendocrine tumors [1]. Our patients in this series had an overall morbidity rate of 43.3% and a 90-day mortality rate of 0.0%, which is consistent with previous evidence and reflects our careful patient selection and multidisciplinary approach [31,32].

Conclusion

Our study presented the indications and outcomes of patients who underwent resection for pancreatic metastases and non-pancreatic, nonneuroendocrine tumors at our high-volume pancreatic surgery center. Our findings show that, when coupled with the low morbidity and mortality rates of a high-volume pancreatic surgery center and good patient selection, pancreatic metastectomy has the potential to result in good long-term survival.

Author contributions

C.L. Stevens, L. Tanno, and D. Karavias conceptualized the project. C.L. Stevens and L. Tanno wrote the original draft. C.L. Stevens, L. Tanno, S.L. China, W.J. Chim, O. Pickering, and D. Karavias performed data curation and data analysis. O. Pickering and D. McDonnell contributed to writing and editing. N.W. Pearce, A. Arshad, A.S. Takhar, T. Armstrong, T.W. Pike, and J.N. Primrose contributed to data curation and project supervision.

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Declaration of competing interest

The authors declare no competing interests.

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