



Pancreatic resection for metachronous colorectal cancer metastases: a case series multicenter study

Francesco Palmieri *, Francesco Lancellotti,[†] Francesco Ferrara ,[‡] Thomas Satyadas,[†] Davide Gobatti,[§] Luis Felipe Abreu de Carvalho,[¶] Filip Gryspeerdt,[¶] Grazia Conte,^{||} Federico Mocchegiani,^{||} Roberto Sampietro[§] and Pierpaolo Sileri*

*Università Vita-Salute San Raffaele, Colorectal Surgery Unit, IRCCS Ospedale San Raffaele, Milano, Italy

[†]Hepato-Pancreato-Biliary Unit, Manchester Royal Infirmary, Manchester, M139WL, UK

[‡]Department of Precision Medicine in Medical, Surgical and Critical Care (Me.Pre.C.C.), University of Palermo, Unit of General and Oncological Surgery, “Paolo Giaccone” University Hospital, Palermo, Italy

[§]Chirurgia Generale Oncologica d’Urgenza, Ospedale Moriggia Pelascini, Gravedona ed Uniti, Italy

[¶]Department of General, HPB and Liver Transplantation, Ghent University Hospital, Gravedona ed Uniti, Belgium and

^{||}Clinica Di Chirurgia Epatobiliare Pancreatica e dei Trapianti, Ospedali Riuniti Delle Marche, Ancona, Italy

Key words

colorectal carcinoma, colorectal metastases, pancreas, pancreas metastases, pancreas resection.

Correspondence

Dr Francesco Palmieri, Università Vita-Salute San Raffaele, Colorectal Surgery Unit, IRCCS Ospedale San Raffaele, via Olgettina 60, 20132 Milano, Italy. Email: palmieri.francesco@hsr.it.

F. Palmieri MD; F. Lancellotti MD;

F. Ferrara MD; T. Satyadas MD; D. Gobatti MD;

L. F. Abreu de Carvalho MD; F. Gryspeerdt MD;

G. Conte MD; F. Mocchegiani MD;

R. Sampietro MD; P. Sileri MD.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

Accepted for publication 29 January 2025.

doi: 10.1111/ans.70027

Introduction

Metastases to the pancreas are quite rare and account for less than 5% of pancreatic malignancies diagnosed in living patients.¹ However, in autopsy cases of malignant tumours, the incidence of pancreatic secondary tumours increases to 15%, underscoring a potentially undiagnosed involvement of pancreas as site for

Abstract

Background: Pancreas resection for **metachronous** colorectal cancer metastasis is episodic and the role of surgery in the management of these patients is still debated.

Methods: We recruited seven patients from three different centres and analyzed 30-day morbidity and mortality, oncological outcomes at 6 and 12 months.

Results: There was no postoperative mortality. Complications occurred in two patients (28,6%). All patients completed at least a 12-months follow-up. At 6-month follow-up, only one patient had a recurrence. At 12-month follow-up, no patients died for disease recurrence and one more patient had a new recurrence.

Conclusion: Our series supports the feasibility and safety of pancreas resection in metastatic colorectal cancer suggesting that radical resection may improve the patient’s prognosis.

metastases.² The metastases are predominantly of epithelial origin, most commonly from lung, stomach, small bowel, colon-rectum, kidney, breast, liver, ovary, melanoma and urinary bladder.^{1,2} It is largely described that resection of isolated metastasis to the lung or liver from primary colorectal tumour leads to improved survival.^{3,4} However, there is no consensus about the benefit of pancreas resection for metastases and the gold standard treatment is still not

well defined. The lack of evidence supporting pancreatic metastasis resections is due to the low incidence and high perioperative risks. Nevertheless, the improvement in morbidity and mortality rates following pancreatoduodenectomy has rendered the indication for this operation more acceptable. Through a retrospectively analysis from different centres, we aim to build a case series to assess the outcomes and potential benefits of pancreatic resection for primary colorectal metastases.

Materials and methods

We launched the study aiming to demonstrate that pancreatic resection for **metachronous** colorectal metastases may be a safe and feasible procedure in selected patients and may provide long-term survival. We sought to address the role of surgical resection and survival benefit from surgery. We suppose to achieve a good prognosis with a median survival close to that observed after resection of hepatic or lung metastases. Patients with isolated **metachronous** pancreatic metastases from colorectal cancer in which the primary tumour was already treated, were included. A preoperative radiological diagnosis of suspected pancreatic metastases from colorectal cancer was achieved in all the patients. Patients with metastases from different malignancies or surgically unresectable lesions were excluded. Aim of surgical interventions was to remove metastases in association to radical lymphadenectomy. Patients' data were retrospectively analyzed and treatment strategies, 90-day morbidity and mortality, oncologic outcomes at 6 and 12 months were evaluated. Surgical morbidity and mortality were recorded within 90 days from the operation, and morbidity was classified according to the classification proposed by Dindo *et al.*⁵ Disease-free survival (DFS) was defined as the time from the pancreatic surgery to disease recurrence or death from any cause. Overall survival (OS) was defined as the time from the pancreatic surgery to death from any cause.

Results

Seven patients from four different surgical centres and three countries were included. Patients' demographics are displayed in Table 1. The mean age was 68.1 years (range 56–80). Two patients underwent a pancreatoduodenectomy, four patients a distal pancreatectomy and one patient underwent a total pancreatectomy.

Only one case was performed by minimally invasive technique. No vein resections were performed in all cases.

The mean time of presentation after the primary tumour was 64.8 months (range 16–147). In six patients the resection was radical (R0) and in one patient the pathologic examination revealed microscopic involvement of posterior margin (R1). In all cases, the pancreatic metastasis showed the same histopathologic features of the primary tumour that was adenocarcinoma. The mean of tumour size was 34.3 cm; the mean lymph nodes harvested was 20.3 (range 7–30) and only two patients had a lymph node involvement. No postoperative mortality was recorded. Complications occurred in two patients (28.6%), one postoperative pancreatic fistula (POPF) grade B and one pulmonary complication, both resolved with conservative treatment and classified as grade I according to Clavien Dindo. The mean of hospital stay was 11.43 (range 7–25). No patients underwent a re-operation. Two patients were readmitted. Chemotherapy after pancreatic resection was administered in 5 patients (all cases except case 4 and case 6); only one patient underwent radiotherapy.

All patients completed at least a 12-months follow-up and six patients had a follow-up longer than 12 months (Table 2). We analyzed the outcome at 6-month follow-up and at 12-month follow-up. At 6-month follow-up, only one patient had a recurrence (case 1, after 2 months) at adrenal gland. This patient had a R1 resection. All patients were alive with good palliation of previous symptoms. At 12-month follow-up, no patients died for disease recurrence and one more patients had new recurrence. Five patients had a recurrence with a mean disease-free survival of 11.2 months until now. If we exclude case that was a R1 resection, no patients had a recurrence in the first 6 months. In the patients that developed recurrence re-operation was no offered.

Table 2 Follow-up summary

	Length of FU (months)	Site of recurrence descriptive (all)	DFS (months)	OS (months)
1	24	Adrenal gland	2	24 (alive)
2	24	Pancreas	16	24 (alive)
3	23	Liver	12	23
4	12	/	12	12 (alive)
5	18	Liver/lymph node	13	18
6	16	Pancreas	16	16 (alive)
7	18	Lymph node	15	18 (alive)

Table 1 Patients' demographic

	Sex	Age at diagnosis	BMI	ASA score	Type of primary surgery	time of presentation (months)	Synchronous resection	Chemotherapy after primary surgery	Pancreas tumour size (mm)	Type of surgery
1	M	64	32.9	2	R-colectomy	43	0	1	45	Distal pancreatectomy
2	M	80	33.9	2	R-colectomy	16	0	1	15	Distal pancreatectomy
3	M	77	22.6	3	R-colectomy	62	0	1	64	Pancreatoduodenectomy
4	M	56	24	2	L-colectomy	85	0	0	22	Distal pancreatectomy
5	F	70	21	3	R-colectomy	39	0	1	30	total pancreatectomy
6	M	68	26.6	3	Rectal anterior resection	62	0	0	38	Distal pancreatectomy
7	M	62	30.9	2	Rectal anterior resection	147	0	1	18	Pancreatoduodenectomy

0 = no 1 = yes.

Discussion

The guidelines for the treatment of colorectal cancer (CRC) recommend resection of hematogenous metastases if they are deemed resectable.⁶ Pancreatic metastases case series are predominantly focused on renal cell carcinoma, and reports of resection for colorectal cancer are sporadic. Limited evidence exists on solitary resected pancreatic metastases originating from colorectal cancer.^{7–11} Therefore, the role of surgery for the management of isolated CRC metastasis is still debated. Pancreatic CRC metastases could occur in a wide range of time. In our series, the mean time of presentation after colon surgery was 64.85 months (range 16–147). One patient reported a metastasis after 147 months from the first diagnosis, underscoring the importance of considering such metastases even long after the primary surgery. The high morbidity and mortality associated to pancreatic resections could discourage surgery for pancreatic CRC metastases. In the current report, two (28.6%) patients experienced a postoperative complication and readmission were recorded in two cases. No perioperative mortality was reported, and this result is consistent with the available literature.^{11–14} Early recurrence occurred in one case, manifesting as a local recurrence in the adrenal gland. Notably, this patient had undergone an R1 resection. Aside from this instance, no other recurrences were observed within the initial 12 months of follow-up, indicating a potential survival advantage in carefully selected cases.

Although some literature suggests that lymph node involvement in pancreatic metastases is unusual and not well defined, in our series two patients (28.6%) showed lymph node metastases suggesting and high percentage of nodes positivity in this kind of localization. Metastases from other cancers (i.e., renal cancer, lung, breast, ovarian, etc.) to the pancreas are much more frequent. The larger series of other metastases show quite long survival after surgery.^{12,15} In a single centre experience, Crippa *et al.* showed that the mean survival time for renal carcinoma was 40.8 months, while the mean survival time of non-renal cell carcinoma was 23 months.¹² Sohn A. T. *et al.* reported the Kaplan–Meier actuarial 5-year survival of 75% in renal cancer metastases.¹³ Reddhy *et al.* showed that the median cumulative overall survival after resection of a pancreatic metastasis was 3.7 years; of note, CRC metastases showed an overall survival of 3.2 years.¹⁶ Although renal cancer is less aggressive than CRC, our study is encouraging pancreatic resection for colorectal cancer. A recent review by Sperti *et al.*, included 37 patients from 24 studies who had pancreatectomy for CRC metastases, showing a median survival time of 21 months.⁸ The small sample of this study doesn't allow to draw definitive conclusions. Moreover, lack of evidence doesn't allow a comparison of these patients with those who did not have a surgical treatment of CRC metastases. More studies and longer follow-up are required to delineate potential benefits of pancreatic surgery for CRC metastases, despite these preliminary results are encouraging. This case series represents one of the extensive series available in the literature. Recruitment for the study is still ongoing, with long-term follow-up pending. Pancreatic resection for CRC metastases remains a viable option in carefully selected patients, offering potential oncological benefits.

Author contributions

Francesco Palmieri: Conceptualization; project administration. **Francesco Lancellotti:** Conceptualization; formal analysis. **Francesco Ferrara:** Data curation. **Thomas Satyadas:** Data curation. **Davide Gobatti:** Data curation. **Luis Felipe Abreu de Carvalho:** Data curation. **Filip Gryspeerdt:** Data curation. **Grazia Conte:** Data curation. **Federico Mocchegiani:** Data curation. **Roberto Sampietro:** Validation; writing – review and editing. **Pierpaolo Sileri:** Supervision.

References

1. Adsay NV, Andea A, Basturk O, Kilinc N, Nassar H, Cheng JD. Secondary tumors of the pancreas: an analysis of a surgical and autopsy database and review of the literature. *Virchows Arch.* 2004; **444**: 527–35.
2. Nakamura E, Shimizu M, Itoh T, Manabe T. Secondary tumors of the pancreas: clinicopathological study of 103 autopsy cases of Japanese patients. *Pathol. Int.* 2001; **51**: 686–90.
3. Weber SM, Jarnagin WR, DeMatteo RP, Blumgart LH, Fong Y. Survival after resection of multiple hepatic colorectal metastases. *Ann. Surg. Oncol.* 2000; **7**: 643–50.
4. Inoue M, Ohta M, Iuchi K *et al.* Benefits of surgery for patients with pulmonary metastases from colorectal carcinoma. *Ann. Thorac. Surg.* 2004; **78**: 238–44.
5. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann. Surg.* 2004; **240**: 205–13.
6. Cervantes A, Adam R, Roselló S *et al.* Metastatic colorectal cancer: ESMO clinical practice guideline for diagnosis, treatment and follow-up. *Ann. Oncol.* 2023; **34**: 10–32.
7. Ishii M, Inoue Y, Matsuo K *et al.* Successful laparoscopic treatment of pancreatic metastasis from sigmoid colon cancer: a case report. *J. Investig. Med. High Impact Case Rep.* 2022; **10**: 23247096221074586.
8. Sperti C, Pasquali C, Berselli M, Frison L, Vicario G, Pedrazzoli S. Metastasis to the pancreas from colorectal cancer: is there a place for pancreatic resection? *Dis. Colon Rectum* 2009; **52**: 1154–9.
9. Matsubara N, Baba H, Okamoto A *et al.* Rectal cancer metastasis to the head of the pancreas treated with pancreaticoduodenectomy. *J. Hepato-Biliary-Pancreat. Surg.* 2007; **14**: 590–4.
10. Konstantinidis IT, Dursun A, Zheng H *et al.* Metastatic tumors in the pancreas in the modern era. *J. Am. Coll. Surg.* 2010; **211**: 749–53.
11. Lee CW, Wu RC, Hsu JT *et al.* Isolated pancreatic metastasis from rectal cancer: a case report and review of literature. *World J. Surg. Oncol.* 2010; **8**: 26.
12. Crippa S, Angelini C, Mussi C *et al.* Surgical treatment of metastatic tumors to the pancreas: a single center experience and review of the literature. *World J. Surg.* 2006; **30**: 1536–42.
13. Sohn TA, Yeo CJ, Cameron JL, Nakeeb A, Lillemoe KD. Renal cell carcinoma metastatic to the pancreas: results of surgical management. *J. Gastrointest. Surg.* 2001; **5**: 346–51.
14. Sperti C, Moletta L, Patanè G. Metastatic tumors to the pancreas: the role of surgery. *World J. Gastrointest. Oncol.* 2014; **6**: 381–92.
15. Z'graggen K, Fernández-del Castillo C, Rattner DW, Sigala H, Warshaw AL. Metastases to the pancreas and their surgical extirpation. *Arch. Surg.* 1998 Apr; **133**: 413–7 discussion 418–9.
16. Reddy S, Edil BH, Cameron JL *et al.* Pancreatic resection of isolated metastases from nonpancreatic primary cancers. *Ann. Surg. Oncol.* 2008; **15**: 3199–206.