Clinical Medicine

# Surgical Re-Resection for Isolated Local Recurrence of Pancreatic Cancer: A Case Series of 3 Patients and Literature Review

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**Abstract**
**Objective.** This retrospective case series study aims to assess the clinical role of surgical re-resection for isolated local recurrence of pancreatic cancer, integrating detailed case presentations with current evidence to clarify patient selection criteria, operative feasibility, and oncologic outcomes. **Case Presentations.** We present three patients with locally recurrent pancreatic cancer who underwent repeat pancreatic resection. Patient 1, who previously underwent distal pancreatectomy for an Intraductal Papillary Mucinous Neoplasm (IPMN)-associated adenocarcinoma, developed a new pancreatic head lesion three years later and underwent pylorus-preserving pancreaticoduodenectomy; histopathology confirmed a small invasive IPMN, and the patient remains alive 8 years after the initial diagnosis and 5 years after the reoperation. Patient 2, who had previously undergone Pylorus-Preserving Pancreaticoduodenectomy for distal bile duct adenocarcinoma, developed recurrent disease in the pancreatic body and tail three years later. He underwent distal pancreatectomy but developed liver recurrence due to hematogenous metastasis one month postoperatively and succumbed 6 months later from generalized widespread disease. Patient 3, who previously underwent a Whipple procedure for IPMN-associated adenocarcinoma, developed a recurrent mass at the pancreatojejunostomy five years later and underwent distal pancreatectomy, with an uneventful recovery. **Conclusion.** Our findings suggest that repeat pancreatic resection may be feasible in carefully selected patients with isolated local recurrence, potentially offering a survival benefit. Strict selection criteria, including the absence of distant metastases, good performance status, and technically resectable disease, appear essential to optimize outcomes, supporting the consideration of surgical re-resection as an option within a multidisciplinary management framework.

**Key Words:** Pancreatectomy ▪ Pancreatic Neoplasms ▪ Repeat Surgery.

## Introduction

Pancreatic cancer is one of the most aggressive malignancies and ranks as the fourth leading cause of cancer-related mortality in both men and women (1, 2). Disease recurrence is common even after initially successful resection, and optimal management of locally recurrent pancreatic cancer remains undefined (3-5). Amidst this lack of consensus, surgical re-resection has historically been underutilized due to technical complexity and limited patient eligibility; however, recent improvements in systematic management have enhanced oncologic control and broadened the applicability of repeat surgery for selected patients (6, 7).

The objective of this study is to present three patients undergoing repeat pancreatic resection, highlighting patient selection, operative feasibility, and oncologic outcomes. The lack of standardized guidelines, as well as a limited amount of published data regarding surgical re-resection for recurrent pancreatic cancer, makes this study clinically relevant.

## Methods

The presented cases were obtained through a thorough retrospective review of the existing medical records. Among a cohort of 350 patients who had initially undergone resection for pancreatic adenocarcinoma, three cases were eligible for reoperation after recurrence. Patients were included in this series after being assessed based on predefined inclusion criteria. Precisely, the evaluation of candidates was focused on patients presenting with the absence of distant metastases, adequate performance status, and technically resectable disease. All of the included cases were discussed in a multidisciplinary tumor board, which reached a consensus for the management approach of each patient. Follow-up methods were conducted based on institutional protocol, which consisted of CT imaging and tumor markers every 6 months for two years, and then annually.

## Case Presentations

### Patient 1

A 59-year-old male patient was found to have a cystic lesion involving the pancreatic body and tail, for which he underwent distal pancreatectomy with splenectomy. Intraoperative exploration revealed no peritoneal or hepatic metastases. The pancreas was transected at the neck, and the spleen was removed en bloc with the distal pancreas. Histopathological examination of the specimen demonstrated a mucinous adenocarcinoma arising in the background of an intraductal papillary mucinous neoplasm (IPMN) of intestinal type with moderate to severe dysplasia. The invasive component measured $4 \times 2.5 \times 4$ cm, confined to the pancreas (pT2N0, AJCC). Resection margins were free of carcinoma, and sixteen regional lymph nodes were negative for metastatic involvement. Six months of adjuvant treatment based on the FOLFIRINOX regimen was established and well tolerated by the patient.

During postoperative yearly follow-up and after 3 years from the initial operation, imaging revealed a new cystic lesion in the pancreatic head, suggestive of a metachronous or multifocal IPMN. The patient subsequently underwent a pylorus-preserving pancreaticoduodenectomy (PPPD) with cholecystectomy. Figure 1 depicts the Computed Tomography (CT) Imaging that the patient underwent in order to show the new lesion (Figure 1).

The resected specimen showed an IPMN of pancreatobiliary type in the pancreatic head, exhibiting low-grade and focal high-grade dysplasia, with a focal area of invasive, moderately differentiated adenocarcinoma measuring <1 cm in greatest dimension. All surgical margins and twelve examined lymph nodes were free of carcinoma (pT1bN0, AJCC). The patient recovered
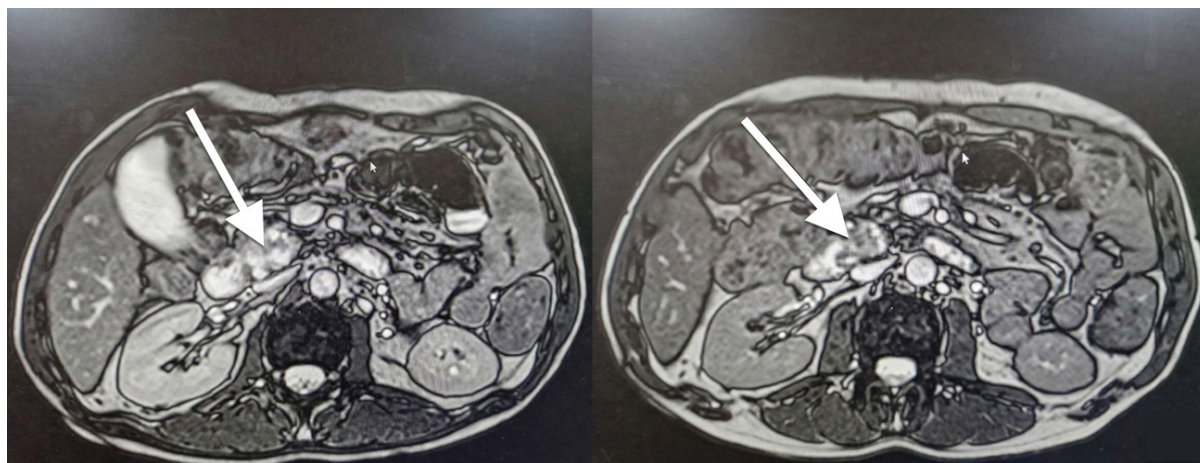


Figure 1. CT of the first patient depicting the new lesion. White arrow showcasing the presence of the lesion on the pancreatic head.

uneventfully following the second operation and is alive and disease-free today, after more than 5 years (~70 months) from the reoperation and 106 months from the initial index surgery.

### Patient 2

A 44-year-old man with a history of gallstone pancreatitis and prior cholecystectomy was found to have an obstructive lesion of the distal common bile duct on magnetic resonance cholangiopancreatography (MRCP). Endoscopic retrograde cholangiopancreatography (ERCP) with stent placement and sphincterotomy was subsequently performed. The patient was discussed in a multidisciplinary tumor board and subsequently underwent PPPD.

Intraoperative findings confirmed a resectable lesion of the distal bile duct. Histopathological evaluation revealed a moderately differentiated adenocarcinoma of the distal bile duct with invasion into the pancreatic parenchyma and focal extension into the peripancreatic fat. Perineural and vascular invasion were present, and one of eighteen lymph nodes demonstrated metastatic involvement. Even though resection margins were negative for carcinoma, a High Grade PanIN was detected at the pancreatic neck margin. The disease was staged as pT3N1 (AJCC). The postoperative course was uneventful, and the patient completed twelve cycles of adjuvant chemotherapy (FOLFIRINOX).

The patient was followed according to institutional protocol, consisting of CT imaging and tumor markers every 6 months for two years, and then annually. Three years postoperatively, the onset of recurrent abdominal pain prompted further investigation. A PET/CT scan revealed a hypermetabolic lesion in the pancreatic tail measuring $2.7 \times 3.3$ cm. Endoscopic ultrasound (EUS) confirmed a focal mass in the pancreatic body with extrapancreatic extension, and fine-needle biopsy suggested recurrent adenocarcinoma. Figure 2 contains the PET/CT scan (Figure 2).

The patient subsequently underwent distal pancreatectomy with splenectomy after discussion and consensus by a multidisciplinary team. Intraoperatively, dense adhesions from the previous Whipple procedure and extensive collateral venous circulation secondary to left-sided portal
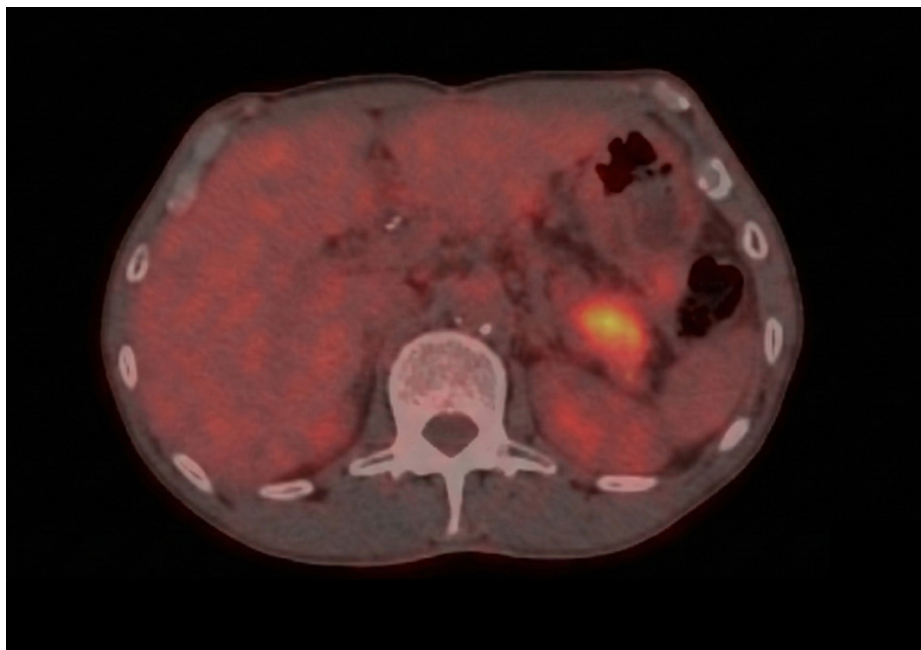


Figure 2. PET/CT scan showcasing the hypermetabolic lesion on the pancreatic body/tail.
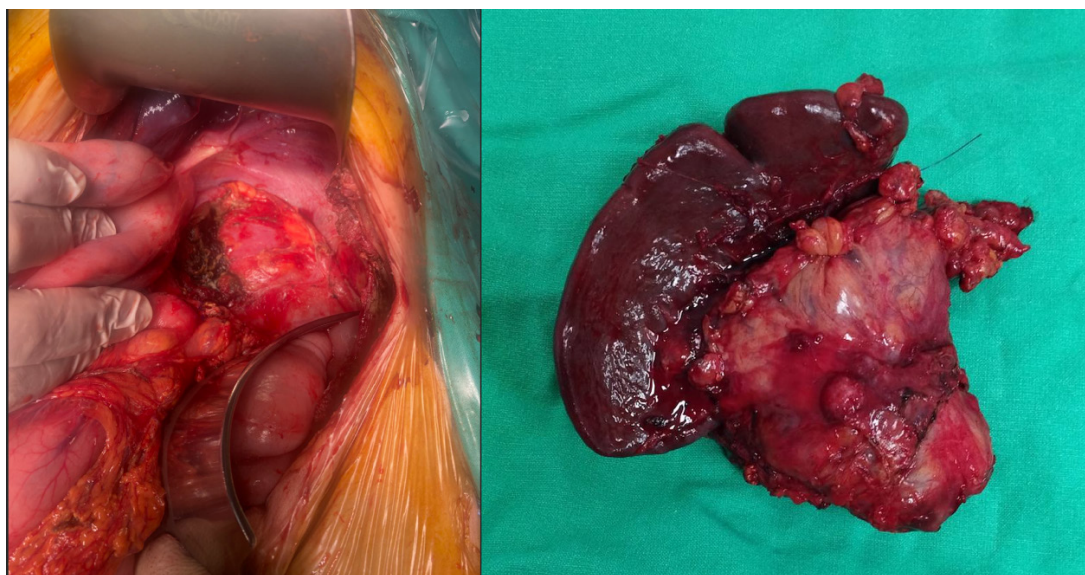
Figure 3. Left: intraoperative image of the distal pancreatectomy of the second patient. Right: specimen removed following the completion of the surgery.

hypertension were encountered, rendering the procedure technically demanding. Figure 3 contains an intraoperative picture (Figure 3).

Histopathology demonstrated a poorly differentiated adenocarcinoma of the pancreatic body and tail, measuring 5 cm in greatest dimension, with vascular invasion and focal extension to the splenic hilum. The anterior surface was microscopically disrupted by tumor infiltration, and two of twenty examined lymph nodes were positive for metastasis (pT2N1). The resection margin contained high-grade pancreatic intraepithelial neoplasia (PanIN). One month later, the patient developed metastatic spread to the liver, and although chemotherapy was offered as a palliative treatment strategy, the patient passed away 6 months later due to widespread disease.

### Patient 3

A 63-year-old man with a history of pancreatic head adenocarcinoma treated with pancreaticoduodenectomy (Whipple procedure) 4 years earlier was referred for surgical management of a newly detected lesion in the pancreatic remnant. The patient had initially undergone a standard Whipple procedure for a moderately differentiated ductal adenocarcinoma of the pancreatic head, arising in association with a mixed-type IPMN exhibiting high-grade epithelial dysplasia. Histopathologic examination revealed tumor extension into the peripancreatic adipose tissue and focal perineural invasion. The pancreatic neck margin contained foci of high-grade IPMN (PanIN-3), whereas the gastric, duodenal, and common bile duct margins, as well as all examined lymph nodes (14 nodes), were free of carcinoma. The tumor was staged as pT2N1 (AJCC). The postoperative course was uneventful, and the patient subsequently received adjuvant chemotherapy based on FOLFIRINOX.

Five years after the index operation, during routine annual surveillance (performed per institutional protocol using CT imaging and tumor markers) and while the patient was asymptomatic, imaging revealed a new mass at the site of the previous pancreatojejunostomy. Operative exploration revealed dense adhesions from the prior surgery. The pancreatojejunostomy and adjacent pancreatic body were carefully dissected, and a distal pancreatectomy with splenectomy was performed, including resection of the splenic hilum.

Histopathologic analysis confirmed a recurrent ductal adenocarcinoma measuring 3.5 cm, located intraparenchymally at the pancreatojejunostomy,

Table 1. Diagnosis, Surgical Management, and Outcomes of the Included Patients

| Parameters | Patient 1 | Patient 2 | Patient 3 |
|---|---|---|---|
| Age | 59 | 44 | 63 |
| Gender | Male | Male | Male |
| Initial Diagnosis | IPMN*-associated adenocarcinoma on the pancreatic body and tail | Distal bile duct adenocarcinoma | IPMN* pancreatic head adenocarcinoma |
| Initial Surgery | Distal Pancreatectomy with splenectomy | PPPD† | Pancreaticoduodenectomy |
| Diagnosis of Recurrence | IPMN* Adenocarcinoma on the pancreatic head | Adenocarcinoma on the pancreatic body and tail | Ductal Adenocarcinoma |
| Surgery for Recurrence | PPPD† | Distal Pancreatectomy with splenectomy | Distal Pancreatectomy with splenectomy |
| Outcome | Alive and disease-free, 70 months postoperatively | Deceased 6 months later | Alive and disease-free, 10 months postoperatively |

*Intraductal Papillary Mucinous Neoplasm; †Pylorus-Preserving Pancreaticoduodenectomy.

without invasion of the jejunal wall. The carcinoma infiltrated and disrupted the anterior pancreatic surface but spared the posterior margin. One lymph node out of 6 were positive for metastatic disease (pT2N1, AJCC). The remaining pancreatic parenchyma demonstrated exocrine atrophy and focal endocrine hyperplasia, while the spleen showed capsular rupture with hemorrhagic changes. All resection margins were free of tumor. The patient recovered uneventfully after surgery and is still alive and disease-free to this day, almost 5 years since the initial operation and 10 months following the second operation. The main characteristics of all 3 patients are presented in Table 1.

## Results

After the assessment of 350 candidates for reoperation, 3 patients (<1%) underwent completion pancreatectomy after being diagnosed with recurrent pancreatic malignancy. The average age of our case series was 55.3 years, while the mean interval between the initial operation and the re-resection was found to be 41.4 months. Patient 3 presented with the greatest time interval between the two operations (50.5 months), which was almost 1.5 times longer than the other 2 cases. Regarding perioperative outcomes, all 3 patients had an uncomplicated course, with no reported morbidities. Histopathological assessment revealed significant variability in tumor burden, with tumor size ranging from <1 cm to 5 cm. Despite this size variation, R0 resection was achieved in all 3 operations. Furthermore, metastatic lymph node involvement was identified in two of the three patients (66%). In terms of long-term oncologic outcomes, results were heterogeneous: one patient succumbed to disease progression at 6 months, while the remaining two patients are alive and disease-free at 70 and 10 months, respectively.

## Discussion

Recurrent pancreatic cancer after initial surgical resection poses a significant therapeutic challenge, as the decision between systemic chemotherapy and surgical reoperation is often complex. In patients with a poor overall prognosis, aggressive interventions may confer more harm than benefit due to the high morbidity (8). However, growing evidence suggests that both chemotherapy and repeat resection can be acceptable management options in selected cases. A systematic review and meta-analysis by Groot et al. reported that while surgical reoperation can be technically demanding, particularly in cases with vascular involvement, it remains an effective and safe therapeutic option when carefully indicated (9). Consistent with the recommendations by Molletta et al., who advised that re-resection should be considered in patients without distant metastases to the liver, lung, bone, or peritoneum, to optimize potential

survival benefit, all three of our patients, who had no evidence of distant metastasis, were carefully selected for reoperation (5). Although multidisciplinary management is often advocated, no standardized international guidelines currently define optimal treatment for this subset of patients (10). Therefore, surgical reoperation should be reserved for patients who fulfill a certain set of criteria, which will be discussed in the next paragraphs.

Our case series illustrates the feasibility of reoperation for locally recurrent pancreatic cancer in three carefully selected patients. Reddy et al., in a large series of over 500 reoperations following pancreatectomy, reported that approximately 1% of all patients underwent late reoperation due to recurrent disease, typically within 1–2 years of the index surgery (11). In contrast, all three of our patients underwent reoperation roughly 3.5 years after their initial procedure, aligning more closely with the pooled analysis by Choi et al., which reported a mean interval of 41.3 months (3.44 years) between the two operations (12).

Several studies have compared outcomes of surgical re-resection versus nonsurgical management. Kleef et al. found that surgical intervention nearly doubled median overall survival (17 vs. 9 months) compared to chemotherapy alone (3). Similarly, Miyazaki et al. demonstrated that the two-year survival was markedly higher in the surgical group (61% vs. 19%), while Serafini et al.'s meta-analysis confirmed a mean overall survival of 29 months and post-recurrence survival of 15 months following reoperation (13, 14).

Comparable results were reported by Yamada et al., who showed a five-year survival increase from 3% in nonsurgical patients to 15% in those who underwent reoperation (15). Kim et al. observed a similar benefit, with median survival of 28 months in surgically treated patients, versus 12 months in those managed non-operatively (16). Strobel et al. further demonstrated that patients with isolated local recurrence achieved a median survival of 26 months compared to 10.8 months with conservative therapy (17). The outcomes of our case series are consistent with the beneficial role of surgical management in survival extension that is reported in the literature, as Patient 1 exceeded the median survival benchmarks of the aforementioned major series. Similarly, it should also be mentioned that Patient 3 remains clinically well and disease-free, 10 months after the operation. Collectively, these studies support the notion that surgery may retain a potentially curative role for highly selected patients with localized recurrence after pancreatectomy (17).

Survival data from recent literature further reinforce the potential benefit of reoperation. Hajibandeh et al., in a systematic review, reported 1-, 2-, 3-, and 5-year survival rates of 70.6%, 38.8%, 20.2%, and 9.2%, respectively (18). Zhou et al. reported slightly higher rates, 82.2%, 49.2%, and 40.6% at 1, 3, and 5 years, respectively, underscoring that selected patients can achieve long-term survival after reoperation for recurrent disease (10).

The divergent postoperative courses of patients 1 and 3, compared to the second patient, highlight the crucial role of prognostic factors in identifying suitable candidates for reoperation. Nienhuser et al. highlighted several favorable indicators: age below 65 years, low BMI (<20 kg/m²), low preoperative CA19-9 levels, completion of adjuvant therapy, R0 resection, and recurrence within the pancreatic remnant, and a long interval (>10 months) since the index resection (6). Favorable molecular subtypes, such as IPMN-associated carcinoma and KRAS- or SMAD4–wild-type tumors, are also linked to improved outcomes (19, 20). All three of our patients exhibited multiple favorable factors, including age <65, long disease-free interval, R0 resection at reoperation, and localized recurrence. Patients 1 and 3 had IPMN-associated tumors, a subgroup generally associated with more indolent behavior. Conversely, patient 2 demonstrated adverse features that are associated with poorer outcomes, such as poor differentiation, vascular and perineural invasion, and nodal metastasis, portending a less favorable prognosis despite technically successful resection. These adverse characteristics may explain the outcome of patient 2, who succumbed to the disease 6 months later. In retrospect, initiation of neoadjuvant chemotherapy could have been a better alternative

Table 2. Data Regarding Survival Benefit of Surgical Reoperation for Recurrent Pancreatic Cancer

| Study | Median Survival for Surgery (months) | Median Survival for non-surgery (months) | 1-year survival | 2-year survival | 3-year survival | 5-year survival |
|---|---|---|---|---|---|---|
| Kleef (3) | 29.0 | 14.5 | - | 67.3 | - | 5.6 |
| Hajibandeh (10) | - | - | 70.6 | 38.8 | 20.2 | 9.2 |
| Serafini (13) | 28.7 | - | - | - | - | - |
| Miyazaki (14) | 25.0 | 9.3 | - | 61 | - | 41 |
| Yamada (15) | 26.0 | 14.0 | - | - | - | 15 |
| Kim (16) | 26.0 | 10.8 | 74.5 | 31.4 | - | 21.7 |
| Strobel (17) | 26.0 | 10.8 | 57.4 | 27.1 | 14.1 | - |
| Zhou (21) | - | - | 82.2 | - | 49.2 | 40.6 |

to upfront surgery. This example showcases the narrow clinical spectrum in which reoperation can be beneficial. Only a few unfavorable characteristics can significantly impact patient prognosis and survival. Detailed data are presented in Table 2.

Although numerous studies report a clear survival advantage for surgical resection in cases of locally recurrent pancreatic cancer, additional factors such as postoperative quality of life, morbidity, and long-term functional outcomes must also be considered (6). Other fundamental factors that guide this decision include the anatomical resectability of the recurrent lesion, the patient's overall performance status, and existing comorbidities (8). Hence, patient selection criteria must not be unidimensional; rather, they require a multifaceted assessment that balances the technical feasibility with the projected quality of life and oncologic outcome.

As discussed earlier, patients with a low likelihood of achieving an R0 resection should not be considered for repeat surgery and are instead better suited for alternative therapeutic approaches. Both the Zhou Y et al. trial (8) and Okusaka et al. (21) review agree that the alternative options of chemoradiotherapy and stereotactic body radiotherapy could act as a useful tool to provide better results for the patient with minimal invasion. Even though the findings of Groot et al.'s review clearly showcase the survival advantage that surgical resection offers, it also highlights the safety and adequate efficacy of the other two options (2). The patients presented in our case series are a prime example of the necessity to apply strict eligibility criteria in order to establish the best possible management approach, as unnecessarily aggressive procedures could significantly impact the patient's prognosis. Therefore, despite the positive data regarding the postoperative trajectory of reoperated patients, the eligibility of such individuals is very limited.

## Conclusion

Our case series contributes to the growing body of evidence by illustrating real-world examples of pancreatic reoperation in carefully chosen patients with isolated local recurrence. These 3 cases, along with their outcomes (positive and negative), indicate that repeat pancreatic resection is feasible and may offer survival benefits in highly selected candidates. However, strict adherence to selection criteria, specifically the absence of distant metastases, preserved performance status, and technical resectability, appears critical to optimizing outcomes. While applicable to a limited patient subset, surgical re-resection warrants consideration as a potentially valuable option within a multidisciplinary management framework. Additional multicenter and prospective studies need to be conducted in order to validate our findings and further refine patient selection criteria.

## What Is Already Known on This Topic:

*Recurrent pancreatic cancer after initial surgical resection is a frequent and clinically challenging scenario, with patients often facing poor overall prognosis. Standard management typically involves systemic chemotherapy or radiotherapy, which can provide disease control but offer limited long-term survival, particularly in cases of isolated local recurrence. Surgical re-resection has historically been underutilized due to its technical complexity, prior operative adhesions, and the limited subset of patients suitable for intervention. However, accumulating evidence demonstrates that reoperation is feasible and can confer meaningful survival benefits when carefully selected patients are treated. Favorable outcomes are generally associated with localized recurrence without distant metastases, good performance status, adequate disease-free interval from the initial surgery, R0 resection, and indolent tumor biology such as IPMN-associated carcinoma. While survival is variable and dependent on individual prognostic factors, selected patients undergoing repeat pancreatic resection can achieve prolonged survival compared to nonsurgical management. High-level evidence regarding the management of locally recurrent disease is limited. Surgical re-resection is a valid option for resectable recurrence, whereas stereotactic radiotherapy and chemoradiation can be considered for unresectable cases.*

## What This Study Adds:

*This study adds real-world evidence on the feasibility and outcomes of repeat pancreatic resection for isolated local recurrence. By presenting three cases with varied pathological features and postoperative courses, it highlights critical factors influencing patient selection, including the absence of distant metastases, favorable tumor biology, long disease-free interval, and technical resectability. The cases illustrate that, when stringent criteria are applied within a multidisciplinary framework, surgical re-resection can be performed safely and may offer meaningful survival benefit for selected patients. Additionally, the study reinforces the limited but potentially curative role of surgery in recurrent pancreatic cancer.*

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**Conflict of Interest:** The authors declare that they have no conflict of interest

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