

**Original Article**

**Combined resection for multifocal lesions of the pancreas**

**Running title: Combined resection of the pancreas**

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**ABSTRACT**

**Background:** Multifocal lesions of the pancreas generally require a total pancreatectomy. However, total pancreatectomy causes severe and permanent pancreatic endocrine and exocrine insufficiency. The aim of this study was to review our experiences of combined resection of the pancreas as an alternative to total pancreatectomy.

**Patients and methos:** From July 2004 to July 2011, 5 patients were indicated to undergo combined resection for multiple lesions of the pancreas at our institution.

**Results:** The surgical procedures for combined resection of the pancreas in the 5 patients consisted of various limited resections of the pancreas. No patient developed insulin-dependent diabetes mellitus. In addition, no patient developed exocrine insufficiency after pancreatic resection.

**Conclusion:** For multifocal lesions of the pancreas, combined resection of the pancreas should be considered the surgical procedure of choice to reduce the risk of both endocrine and exocrine insufficiency.

**KEY WORDS:** Combined resection, Multifocal lesions, pancreatic duct navigation surgery

**ABBREVIATIONS:** duodenum-preserving pancreatic head resection (DPPHR); medial pancreatectomy, and middle-preserving pancreatectomy (MPP); intraductal papillary-mucinous neoplasm (IPMN); endocrine tumor associated with multiple endocrine neoplasia syndrome type 1 (MEN1); Computed tomography (CT); renal cell carcinoma (RCC); Endoscopic retrograde pancreatography (ERP); distal pancreatectomy (DP); Magnetic resonance cholangiopancreatography (MRCP); endoscopic naso-pancreatic drainage (ENPD)

## **Introduction**

Recently, several improvements in surgical devices and advances in knowledge of the pancreatic anatomy have allowed surgeons to approach the limited resection of the pancreas, such as partial pancreatectomy, duodenum-preserving pancreatic head resection (DPPHR), medial pancreatectomy, and middle-preserving pancreatectomy (MPP) (1-4). On the other hand, although several surgical techniques and devices have been advocated to avoid complications following pancreatic surgery, the incidence of pancreatic fistula is still high (5, 6). In particular, the incidence of pancreatic fistula following limited resection of the pancreas is high (7). A pancreatic fistula is one of the most frequent complications and is still responsible for most morbidity and mortality after pancreatic surgery, because it causes lethal bleeding (8, 9). Therefore, several surgical techniques such as main pancreatic duct ligation, prolamine injection, fibrin glue sealing, pancreatic duct navigation surgery, and the gastric wall-covering method have been advocated to prevent the pancreatic fistula (10-14).

Many benign and low-grade malignant pancreatic lesions,

including intraductal papillary-mucinous neoplasm (IPMN), have been detected by using the improved diagnostic modalities. IPMNs are classified into 2 types according to their site of occurrence: the main-duct type and branch-duct type (15). Branch-duct type IPMN is often multifocal (16). In addition, it is well known that patients with IPMN are at an increased risk of pancreatic ductal carcinoma. Yamaguchi et al. (17) reported that 7 of their 76 (9.6%) patients with IPMN showed invasive ductal carcinoma of the pancreas. Other multifocal diseases of the pancreas commonly occur in endocrine tumor associated with multiple endocrine neoplasia syndrome type 1 (MEN1) and metastatic renal cell carcinoma (18, 19). In these patients with multifocal lesions of the pancreas, total pancreatectomy is generally used as a choice of surgical treatment. However, total pancreatectomy causes a poor quality of life postoperatively, with severe and permanent pancreatic endocrine and exocrine insufficiency.

Herein, we report our experiences of 5 patients who underwent combined resection including several limited resections of the pancreas for multifocal lesions of the pancreas.

**Patients, preoperative findings, and surgical procedures**

From July 2004 to July 2011, 5 patients were indicated to undergo combined resection for multiple lesions of the pancreas at our institution (Table 1). There were 2 men and 3 women with a mean age of 63 years (range, 52-81 years). The preoperative findings of multiple lesions of the pancreas, diagnoses and surgical procedures for each case were as follows:

*Case 1*

Computed tomography (CT) showed four masses in the pancreas: one in the uncinate process and the others in the body and tail of the pancreas (Figure 1a, 1b). Angiography demonstrated hypervascular masses in the pancreas, corresponding to the CT findings. This patient underwent right radical nephrectomy for renal cell carcinoma (RCC) 6 years ago, and metastatic pancreatic tumors from RCC were diagnosed. She underwent combined resection consisting of a partial resection at the uncinate process and a distal pancreatectomy (DP). Her postoperative course was uneventful.

*Case 2*

CT showed two multilobular cystic lesions, 15 mm and 40 mm in

diameter, respectively, in the head and body of the pancreas. Endoscopic retrograde pancreatography (ERP) showed two cystic lesions communicating with the main pancreatic duct, and the main pancreatic duct showed no abnormalities. Magnetic resonance cholangiopancreatography (MRCP) and ERP revealed a communicating branch to these two cystic lesions. No mural nodules were noted in the cysts by either diagnostic modality. This patient was diagnosed with multiple branch-duct type IPMNs in the head and body of the pancreas. He underwent partial resection for two IPMNs under intraoperative pancreatography using an endoscopic naso-pancreatic drainage (ENPD) tube to avoid injury to the main pancreatic duct when performing partial pancreatic resection. His postoperative course was uneventful.

### *Case 3*

CT showed two multilobular cystic lesions, 40 mm and 30 mm in diameter, respectively, in the uncinate process and tail of the pancreas. No mural nodules were noted in the cysts. The main pancreatic duct of the head of the pancreas was dilated 10 mm in diameter. This patient was diagnosed with main-duct type IPMNs in the head of the pancreas and branch-duct type IPMN in the tail

of the pancreas. She underwent MPP consisting of DPPHR and DP. Her postoperative course was uneventful.

*Case 4*

CT showed a multilobular cystic lesion 45 mm in diameter in the uncinate process of the pancreas. No mural nodules were noted in the cyst. In addition, a nodule 20 mm in diameter was detected in the body of the pancreas. MRCP showed a cystic lesion in the uncinate process of the pancreas, which was communicating with the main pancreatic duct, and the main pancreatic duct showed obstruction in the body of the pancreas (Figure 2). This patient was diagnosed with a pancreatic carcinoma in the body of the pancreas with a branch-duct type IPMN in the uncinate process of the pancreas. She underwent partial resection of the uncinate process and DP under an intraoperative pancreatography using an ENPD tube to avoid injury to the main pancreatic duct when performing partial pancreatic resection of the uncinate process. Her postoperative course was uneventful.

*Case 5*

CT showed a solid mass 15 mm in diameter in the head of the pancreas. In addition, a cystic mass 20 mm in diameter was detected in the

tail of the pancreas. In addition, this patient showed a parathyroid tumor, and pancreatic endocrine tumors associated with MEN1 were diagnosed. He underwent MPP consisting of pancreatic head resection with segmental deodenectomy and DP. He had a grade B postoperative pancreatic fistula. Individual patient data are shown in Table 1.

**Follow-up results and prognosis (Table 2)**

The median follow-up period after surgery was 58 months (range, 26-97 months). No patient developed insulin-dependent diabetes mellitus. The preoperative median HbA1c level was 5.1% (range, 4.9-5.3%), and the postoperative median HbA1c level was 5.4% (range, 4.9-6.0%). On the other hand, no patient developed exocrine insufficiency after pancreatic resection. The preoperative median BT-PABA test was 63.7% (range, 40.0-71.1%), and the postoperative median HbA1c level was 61.8% (range, 42.9-74.8%). Two patients died of liver metastases. One patient is alive with liver and bone metastases. Two patients are alive and disease free.

## **Discussion**

In the present series, we performed combined resection of the pancreas for the following 5 combinations of tumors: metastatic tumors; branch-duct type IPMNs; main-duct type IPMN and branch-duct type IPMN; branch-duct type IPMN and pancreatic carcinoma; and endocrine tumors.

Total pancreatectomy is usually considered for multifocal metastatic tumors of the pancreas. However, total pancreatectomy results in severe and permanent endocrine and exocrine pancreatic insufficiency due to a total loss of normal pancreatic parenchyma. The present case 1 showed multifocal pancreatic metastases from RCC located in the uncinate process, body and tail of the pancreas, which is usually an indication for total pancreatectomy. On the other hand, several reports have demonstrated that partial resection of the pancreas with a cancer-free margin is the optimal surgical strategy for pancreatic metastases from RCC (20, 21). The effectiveness of pancreatic resection for the pancreatic metastases is dependent on the malignant potency of the primary cancer, and pancreatic metastases from RCC show the most favorable outcome (21). Although a non-standardized pancreatic resection

such as combined resection is a controversial strategy for the treatment of multifocal pancreatic metastases from RCC, we selected a combined resection that consisted of a partial pancreatic resection and distal pancreatectomy rather than a total pancreatectomy in order to preserve the normal pancreatic parenchyma in our case 1.

In our series, 3 patients with branch-duct type IPMN underwent combined resection of the pancreas. Branch-duct type IPMN has been recognized as a mucin-producing cystic neoplasm with a favorable prognosis (15). In addition, branch-duct type IPMN includes variable histological grades from hyperplasia to adenocarcinoma (15). In the benign or low-grade malignant IPMN, complete tumor resection is sufficient for a cure. Due to the less aggressive biologic behavior of branch duct IPMNs, we propose that multifocal branch-duct type IPMN or the combination of branch-duct type IPMN and another pancreatic disorder is a good candidate for combined resection of pancreas. On the other hand, 1 of the present patients had a combination of main-duct type and branch-duct type IPMN and underwent combined resection of the pancreas to avoid total pancreatectomy. Our recent study has demonstrated that total

pancreatectomy for the main-duct type IPMN should be considered mainly for cases with a malignant lesion spreading to the whole pancreas (22).

In patient no. 5 of the present series, who exhibited multifocal endocrine tumors in MEN 1, we chose a combined PHRSD and DP rather than a total pancreatectomy in order to avoid severe and permanent endocrine and exocrine pancreatic insufficiency. The combination of pancreatic head resection and pancreatic tail resection is known as the MPP. Several recent reports have described that MPP is a feasible procedure for multicentric neoplasms of the pancreas including endocrine tumors and might reduce the risk of both endocrine and exocrine insufficiency (4, 23).

In 3 patients, we chose a partial resection of the pancreas as one of the combined resections. Partial resection of the pancreas is ultimately a less invasive surgical procedure for benign or low-grade malignant neoplasms of the pancreas, which is most suitable for the preservation of pancreatic functions. However, there is a high incidence of complications following partial resection of the pancreas, including pancreatic fistula

(7). To avoid pancreatic fistula following partial resection of the pancreas, we have proposed pancreatic duct-navigation surgery using an ENPD tube (13). Pancreatic duct-navigation surgery enables us to prevent intraoperative injury to the main pancreatic duct during intraoperative pancreatography by using an ENPD tube.

In summary, the routine performance of total pancreatectomy for the treatment of multifocal lesions in the pancreas is not acceptable. Therefore, for multifocal lesions of the pancreas including a benign or low-grade malignant lesion, combined resection of the pancreas should be considered the surgical procedure of choice to reduce the risk of both endocrine and exocrine insufficiency when technically appropriate.

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**Figure legends**

**Figure 1** Enhanced abdominal computed tomography findings in the patient with multifocal lesions of metastatic pancreatic tumors from renal cell carcinoma. Well-enhanced masses in the uncinete process (a), and body (b) of the pancreas.

**Figure 2** MRCP showed a cystic lesion in the uncinete process of the pancreas (arrowhead), and the main pancreatic duct showed an obstruction in the body of the pancreas (arrow).

Figure 1 (a)

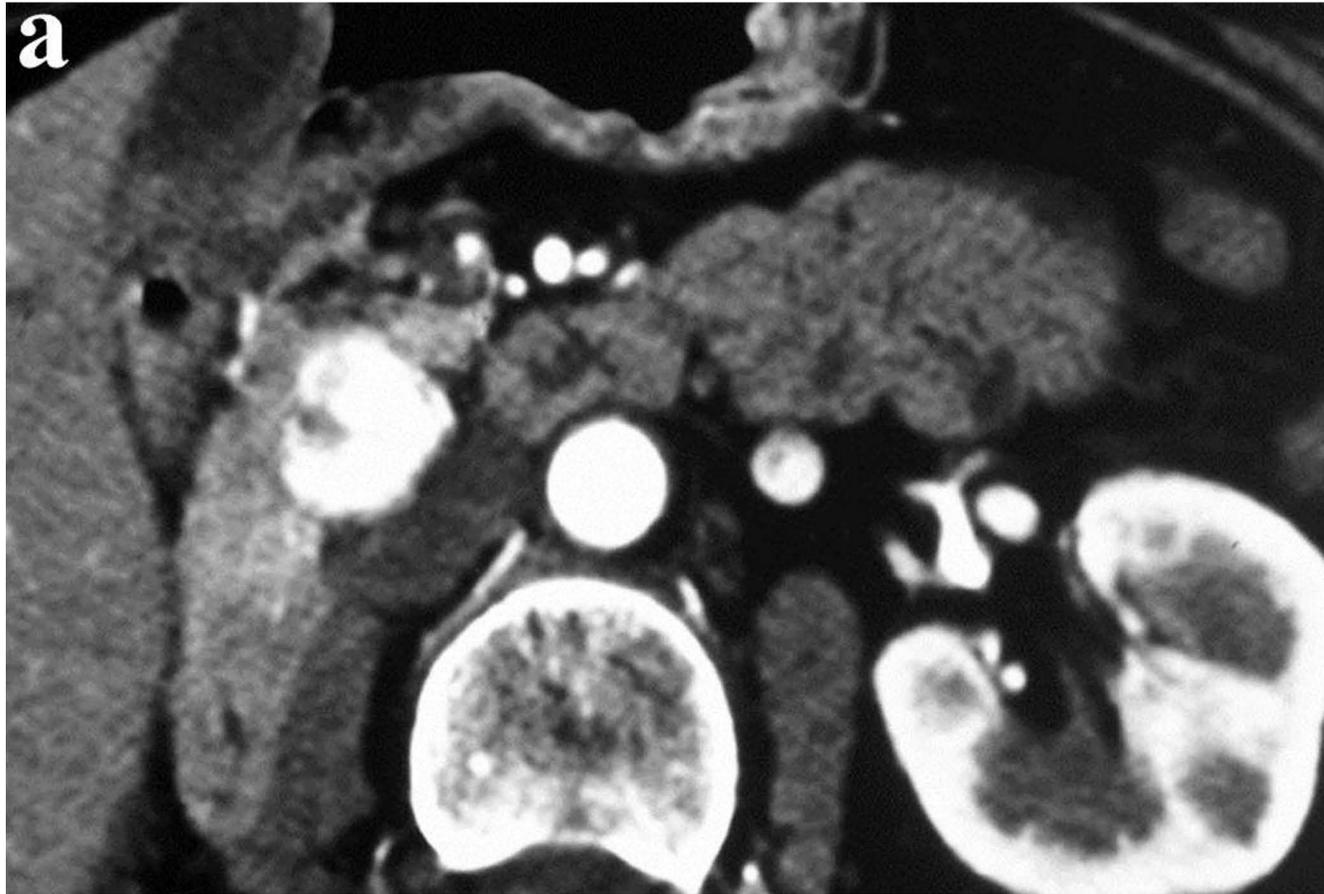


Figure 1 (b)



Figure 2

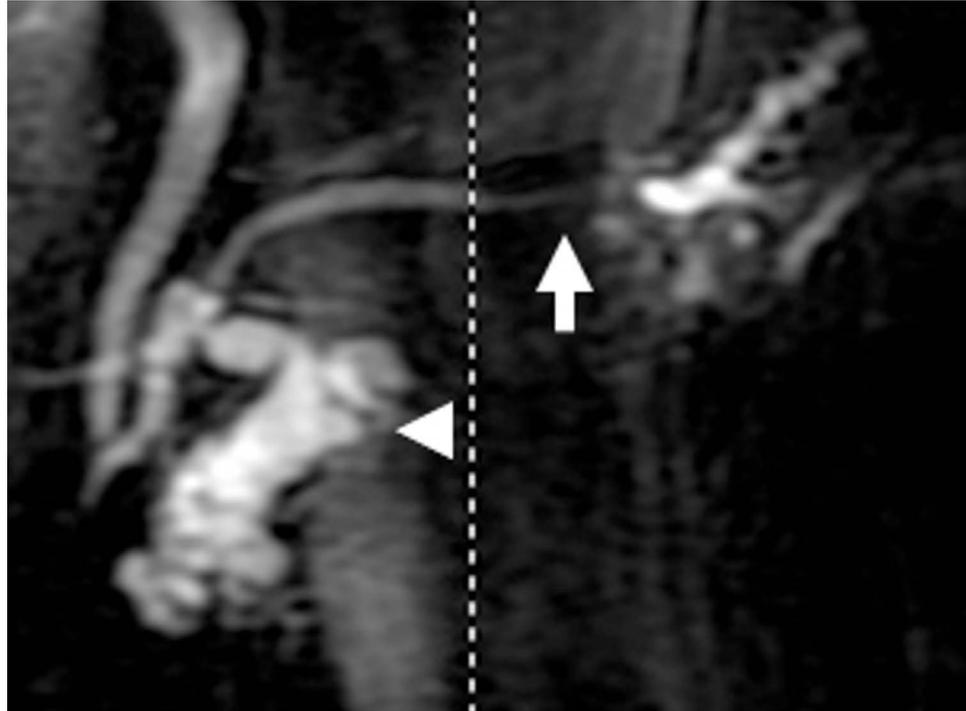


Table 1. Clinical features of four cases of combined resection for multiple lesions of the pancreas

Case	Age(y)/Sex	Diagnosis and findings of multiple lesions of the pancreas	Operation
1	67/F	head: metastatic tumor; body and tail: metastatic tumor	PR (uncinate process), DP
2	56/M	head: branch-duct type IPMN; body: branch-duct type IPMN	PR (uncinate process, body)
3	79/F	head: main-duct type IPMN; tail: branch-duct type IPMN	DPPHR, DP
4	59/F	head: branch-duct type IPMN; tail: pancreatic carcinoma	PR (uncinate process), DP
5	52/M	head: endocrine tumor; tail: endocrine tumor	PHRSD, DP

IPMN, intraductal papillary mucinous neoplasm; PR, partial resection; DP, distal pancreatectomy;

DPPHR, duodenum-preserving pancreatic head resection; PHRSD, pancreatic head resection with segmental duodenectomy.

Table 2. Follow-up results and prognosis

Case	HbA1c (%)		BT-PABA test (%)		Prognosis (mo)
	Before operation	After operation	Before operation	After operation	
1	5.1	4.9	63.7	63.6	Liver and bone metastases, 97
2	4.9	5.0	67.8	74.8	Disease free, 77
3	5.3	5.6	40.0	60.0	Death from liver metastases, 37
4	5.0	5.4	71.1	ND	Death from liver metastases, 26
5	5.2	6.0	63.0	42.9	Disease free, 58

HbA1c, hemoglobin A1c; BT-PABA, *N*-benzoyl-tyrosyl-*p*-aminobenzoic acid; ND, not done.