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Original paper

# Pylorus-preserving total pancreatectomy for an intraductal papillary-mucinous neoplasm of the pancreas

Mitsuhiro Inagaki[1], Mitsuhiro Obara[1], Shuichi Kino[1], Junichi Goto[1], Shigeki Suzuki[1], Akira Ishizaki[1], Satoshi Tanno[2], Yutaka Kohgo[2], Yoshihiko Tokusashi[3], Naoyuki Miyokawa[3], and Shinichi Kasai[1]

[1]Department of Surgery, Asahikawa Medical College, Midorigaoka-Higashi 2-1-1-1, Asahikawa, 078-8510 Japan

[2]Department of Medicine, Asahikawa Medical College, Asahikawa, Japan

[3]Department of Surgical Pathology, Asahikawa Medical College, Asahikawa, Japan

Corresponding address to Mitsuhiro Inagaki, Department of Surgery, Asahikawa Medical College, Midorigaoka-Higashi 2-1-1-1, Asahikawa, 078-8510 Japan

Tel: 81-166-68-2503, Fax: 81-166-68-2193, e-mail: inagaki@asahikawa-med.ac.jp

A short title: Pylorus-preserving total pancreatectomy for IPMN

Key words: pancreas, pylorus-preserving total pancreatectomy, intraductal papillary-mucinous neoplasm, fatty liver

**Abstract**

*Background/Purpose.* A total pancreatectomy (TP) is rarely performed to treat invasive ductal carcinoma of the pancreas due to the associated markedly impaired quality of life and poor prognosis after the resection. Intraductal papillary-mucinous neoplasm (IPMN) of the pancreas is characterized by an extensive intraductal spread and a favorable outcome even when presenting at an invasive stage. We herein reappraise the role of a pylorus-preserving total pancreatectomy (PPTP) as a viable alternative pancreatic resection modality for borderline and malignant IPMN.

*Methods.* A total of five patients with IPMN underwent PPTP and their clinical follow-up data were reviewed.

*Results.* TP was performed due to recurrent IPMN in the remnant pancreas after distal pancreatectomy in three patients and due to massive involvement of the entire pancreas in the others. All patients were treated by the pylorus-preserving method, while the spleen was also preserved in one patient. The surgical margins were negative and no metastasis to the resected lymph nodes was evident based on histological examinations. One patient underwent a re-operation due to postoperative intra-abdominal bleeding while another patient required tube-drainage for left pleural effusion. Three out of four patients who underwent PPTP with a splenectomy experienced postoperative gastric ulcer which were controlled by medication. One patient was died due to suicide at 16 months after PPTP. All others were doing well without recurrence at from 62 months to 127 months after PPTP.

*Conclusions.* PPTP is therefore considered to be indicated as an effective treatment for borderline or malignant IPMN with extensive involvement when the patient's condition permits in order to obtain a complete resection of the IPMN.

## Introduction

Total pancreatectomy (TP) used to be recommended for the treatment of pancreatic cancer in the 1960s and 70s because of the multicentricity of the cancer lesion in the pancreas and the frequent presence of extensive lymph node metastasis (1 - 3). Recently, this procedure is no longer the standard modality for the treatment of pancreatic cancer and it is now only performed in selected patients because of infrequent multicentricity, and the associated marked decrease in the quality of life with only a slight survival benefit after the resection (4 – 7). Intraductal papillary-mucinous neoplasm (IPMN) has unique characteristics such as marked dilatation of the pancreatic duct filled with excessive mucin and a favorable prognosis in contrast to the prognosis for invasive ductal carcinoma of the pancreas (8 – 10). According to the degree of epithelial dysplasia in IPMN lesions based on a histological examination, IPMN may be classified as either adenoma, a borderline tumor or carcinoma. In addition, some of IPMN also demonstrate multicentricity of the lesion in the pancreas (11, 12). A resection of IPMN is only possible in tumors limited to the head or body-tail of the pancreas in which an intraoperative frozen section examination reveals no further spread of the tumor along the main pancreatic duct beyond the resection line (13). Recently, international consensus guidelines for management of IPMN and mucinous cystic neoplasms of the pancreas have been published (14). In cases where the tumor appears to involve the entire pancreatic duct from the ampulla to the tail or a recurrence of IPMN is detected in the remnant pancreas, TP has to be performed to ensure the removal of all lesions. However, such an aggressive approach has to be carefully weighed against the risk of the operation and the postoperative problems arising with a complete loss of the endocrine and exocrine functions. We herein reappraise PPTP as

a viable alternative pancreatic resection modality for borderline and malignant IPMN.

**Patients and methods**

A total of 65 Japanese patients with IPMN were treated in the Department of Surgery, Asahikawa Medical College Hospital, Asahikawa Japan, form March 1990 up to April 2006. Out of these 65 patients, five patients underwent a pylorus-preserving total pancreatectomy (PPTP). The indications for a total pancreatectomy were recurrent IPMN in the remnant pancreas after a distal pancreatectomy for either borderline or malignant IPMN in three (patients 1, 2, and 4) and massive involvement of the entire pancreas in two (patients 3 and 5) (Table 1 and 2).

The clinical charts were reviewed concerning the such preoperative data as below; age, sex, chief complaint, presence or absence of mucin hypersecretion, tumor markers including the carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9) levels, serum chemistry including the 75g glucose tolerance test, cytology of the pancreatic juice, the imaging findings, indications for PPTP, operative findings, and histological diagnosis of the resected specimen and dissected lymph nodes. The follow-up data of the presence or absence of gastric ulcer, fatty liver, and diabetic retinopathy, follow-up imaging and change of body weight were obtained in all five patients and then were updated as of May 2006.

**Results**

**Patients**

The five patients comprised three men and two women and the age at PPTP ranged from 59 to 74 years (Table 1). The chief complaint was epigastric pain in three patients and back pain in one patient. The serum CA19-9 levels were not elevated in

any of the five patients but the CEA level was elevated in two patients. One of five patients showed a borderline disturbance on the glucose tolerance test, while the others demonstrated a diabetic pattern. A cytological analysis of the pancreatic juice showed adenocarcinoma in one patient.

Follow-up imaging showed a dilatation of the residual main pancreatic duct with the appearance of mural nodules therein, thus suggesting a recurrent of IPMN (Figure 1). Imaging showed a diffuse marked dilatation of the main pancreatic duct with mural nodules observed in two patients (Figures 2 - 4). Thereafter, total resection of the remaining pancreatic head was performed, thus resulting in a TP.

**Operation**

All 5 patients underwent PPTP while the spleen was also preserved in one patient (patient 5) (Table 2). The coronary vein form the stomach was preserved in four patients except patient 4. Two patients underwent a resection of the rest pancreas at 5 (patent 1) and 8 (patient 2) years after the distal pancreatectomy. The other patient (patient 4) had resection of the body in the pancreas at 2 years after the distal pancreatectomy while 2 years after the second operation, he finally underwent PPTP due to a recurrence of IPMN in the remnant pancreas.

**Histopathologic Diagnosis**

The histopathological diagnosis of the resected specimen was non- invasive intraductal papillary-mucinous carcinoma in two patients (patients 1 and 4) and invasive carcinoma derived from IPMN in one patient (patient 3) (Table 2). In the other two (patients 2 and 5), the diagnosis was borderline IPMN with severe dysplasia. Both the lymph nodes and surgical margins were free of cancer cells in all patients.

**Clinical Outcome**

After PPTP, one patient (patient 1) had a re-operation due to postoperative intra-abdominal bleeding. Another patient (patient 3) demonstrated left pleural effusion which thus required tube drainage. Three out of four patients who underwent PPTP with a splenectomy experienced postoperative gastric ulcers which were controlled by medication (Table 3). All patients were required insulin injection while hypoglycemia was rare in all four patients. One patient (patient 1) died due to suicide at 16 months after PPTP. The four remaining patients were all doing well from 62 months to 127 months after PPTP. The body weight at discharge was lower than before the operation, but it recovered to pre-operative level by 6 months after PPTP (Figure 5).

**Discussion**

The five patients with borderline or malignant IPMN that underwent PPTP in our hospital were reviewed. TP was employed for the remnant pancreas after a distal pancreatectomy for borderline or malignant IPMN in three patients and massive involvement of the entire pancreas with malignant IPMN in the others. The surgical margins were negative and no lymph node metastases were evident in any patients based on a histopathological examination. One patient died due to suicide at 16 months after PPTP. All others were doing well from 62 months to 127 months after PPTP with no signs of recurrence. We therefore consider that PPTP can be safely performed in these patients with IPMN.

The characteristic features of IPMN have been described as extensive intraductal spread, multicentricity, and frequent concomitant invasive ductal carcinoma at a site distant from the IPMN lesion (12). A total resection of IPMN guided by frozen section

in order to avoid residual IPMT during the operation is required (13). Therefore, TP for patients with IPMN is considered to be indicated when a surgical margin is positive intraoperatively and it is theoretically thought to be the most appropriate modality for performing a complete resection of IPMN (15, 16). However, more limited subtotal resections may also be considered depending on the patient's age, the presence of medical commodities and psychosocial factors. Previously, a few reports have described a radical resection to cure periampullary tumors to be safe for selected elderly patients (17).

In the 1990's, Karpoff et al. reviewed their experience with TP for adenocarcinoma of the pancreas (6). TP could thus be performed safely with a low mortality, while the survival was predicted based on the underlying pathologic findings. Patients undergoing TP for adenocarcinoma had a uniformly poor outcome, which thus led many to bring into question the value of this operation. Therefore, TP is considered to be indicated for patients with IPMT, not for those with invasive ductal carcinoma, because the clinical course of patients with IPMN is favorable even though it is an invasive type. Recently, Yamaguchi et al. reported that TP should be indicated for the treatment of benign or malignant IPMN with extensive involvement when the patients' condition permits since it provides the best chance of cure (18).

Various types of organ-preserving TP have been proposed; including pylorus-preserving (19, 20), duodenum-preserving TP (21, 22), subtotal duodeno-pancreatectomy (23) and spleen preserving TP (24 – 26). Sugiyama et al. compared standard TP and PPTP for both pancreatic adenocarcinoma and intraductal-mucinous carcinoma (19). Early morbidity and mortality did not differ substantially between the two groups but late complications, including uncontrollable

diabetes, diarrhea and malnutrition tended to occur less frequently after standard TP. The serum albumin and body weight at six months after surgery were significantly higher in PPTP than in standard TP. Regardless of the tumor type, the long-term survival rates did not differ significantly between the two groups. They concluded that PPTP for pancreatic cancer improves the nutritional recovery without compromising the long-term survival in comparison to the standard TP. Some organ-preserving TP should be considered for patients with IPMN depending on the extension of the lesion, although the number of the patients was small in this series.

Little information has been reported on the metabolic characteristics of the totally pancreatectomized patients or the efficacy of medical management after radical pancreatic surgery. Another metabolic disturbances, other than the pancreatic exocrine and endocrine functions, is the occurrence of fatty liver (27). Dresler et al. reported that three patients developed fatty liver from approximately three years after PPTP (28).

PPTP should therefore be considered for the treatment of IPMN in order to obtain a complete removal for the lesion when the patient’s conditions permit, however, a careful long-term follow-up is essential in such cases.

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**Figure legends**

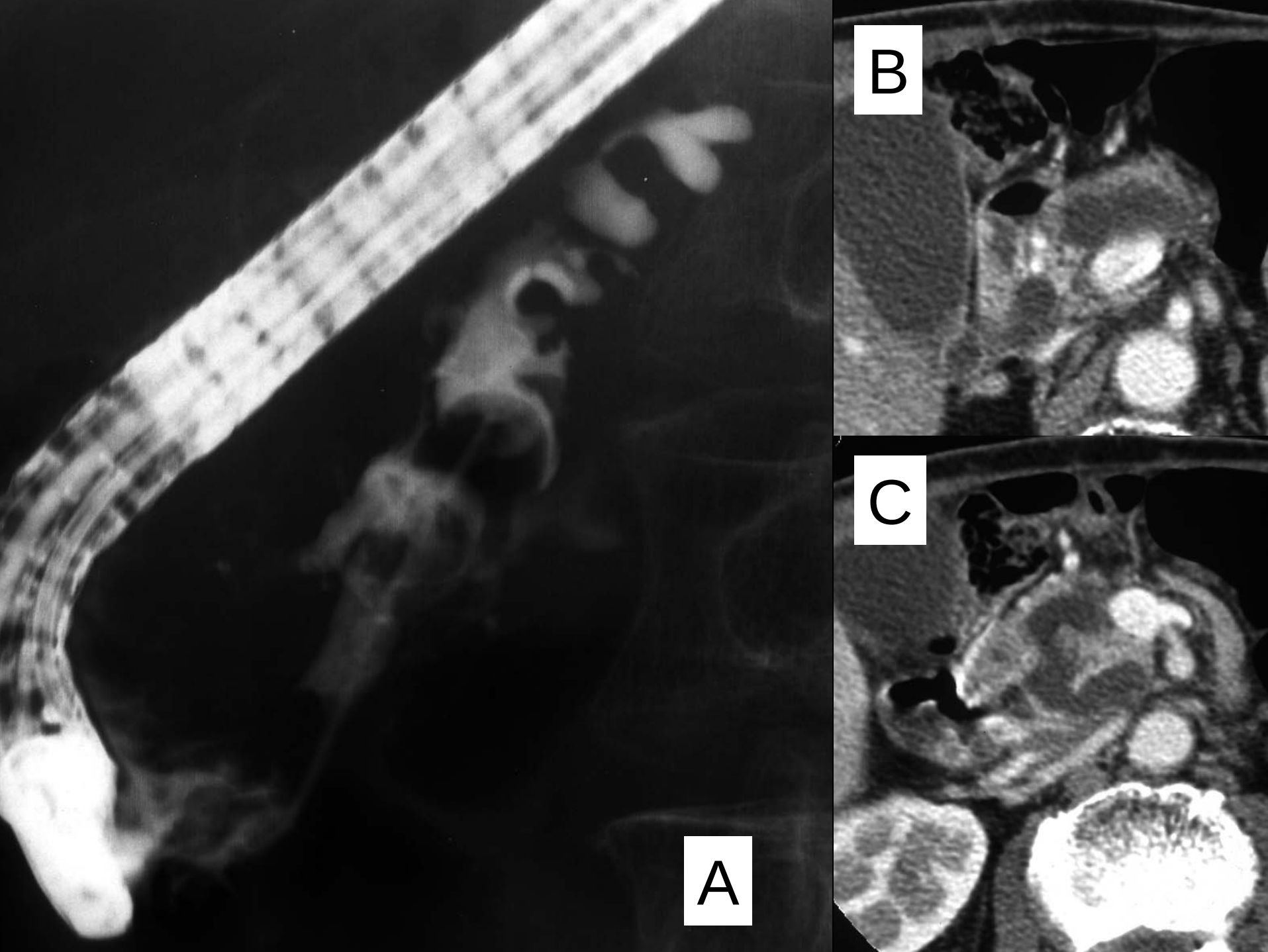
Figure 1. (A) Endoscopic retrograde pancreatography of the remnant pancreas shows a marked dilatation of the main pancreatic duct with mural nodules (patient 4). (B, C) CT also shows a marked dilatation of the main pancreatic duct.

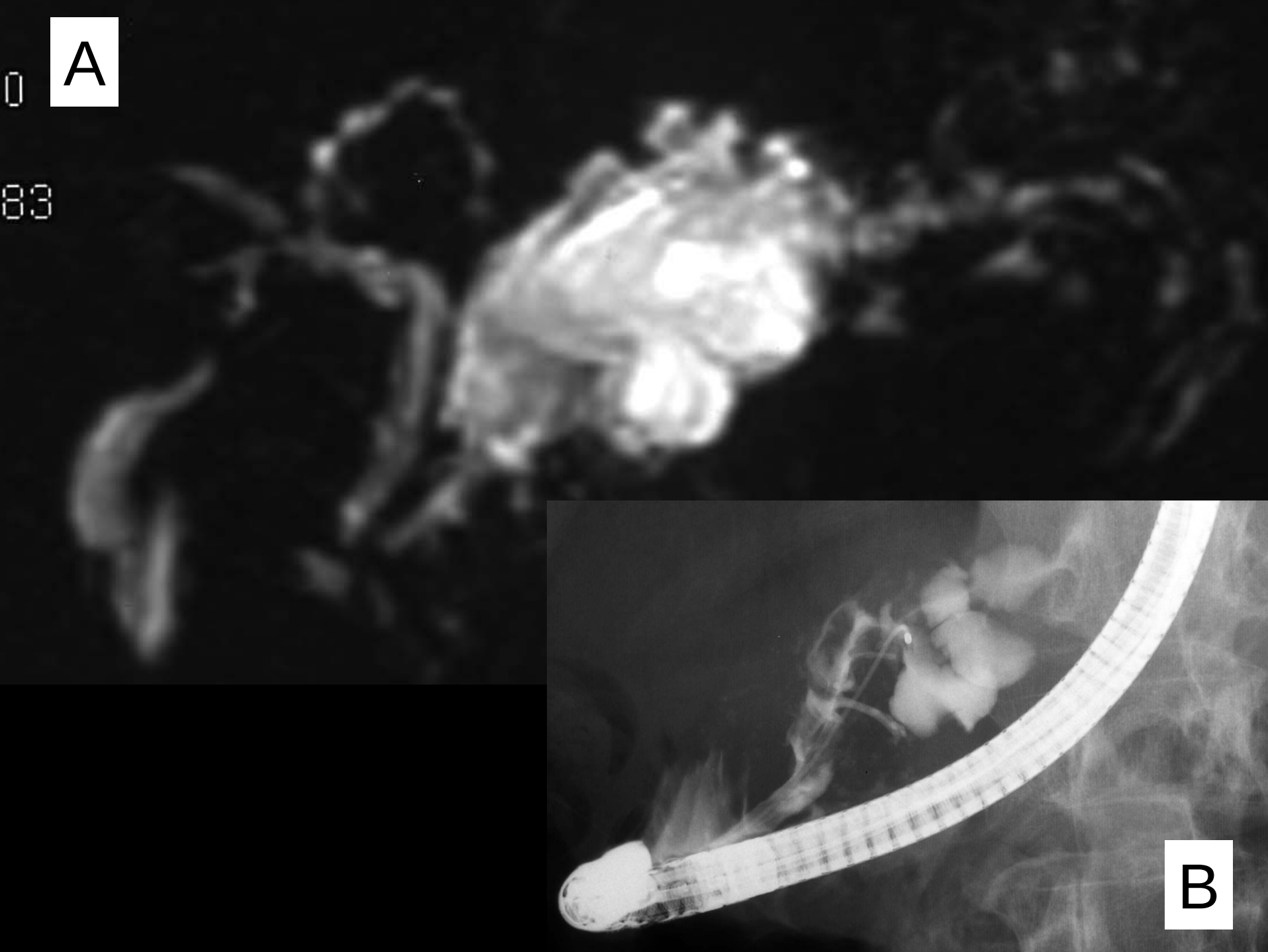
Figure 2. (A) MRCP shows marked dilatation of the main pancreatic duct (patient 5). (B) Endoscopic retrograde pancreatography shows a marked dilatation of the main pancreatic duct with mural nodules.

Figure 3. (A, B) CT also shows a marked dilatation of the main pancreatic duct.

Figure 4. (A) The view after a distal pancreatectomy with spleen-preservation. (B, C) Macroscopic findings of the resected pancreas. (D) Microscopic findings of the tumor. H&E, X200.

Figure 5. Postoperative change in body weight. To avoid comparing people with different body mass, the body weight of each patient was standardized by referring to the preoperative level as 100%. Body weight at discharge was lower than before the operation, but recovered to the pre-operative level by 6 months after PPTP.


A
B
C


A
0
83
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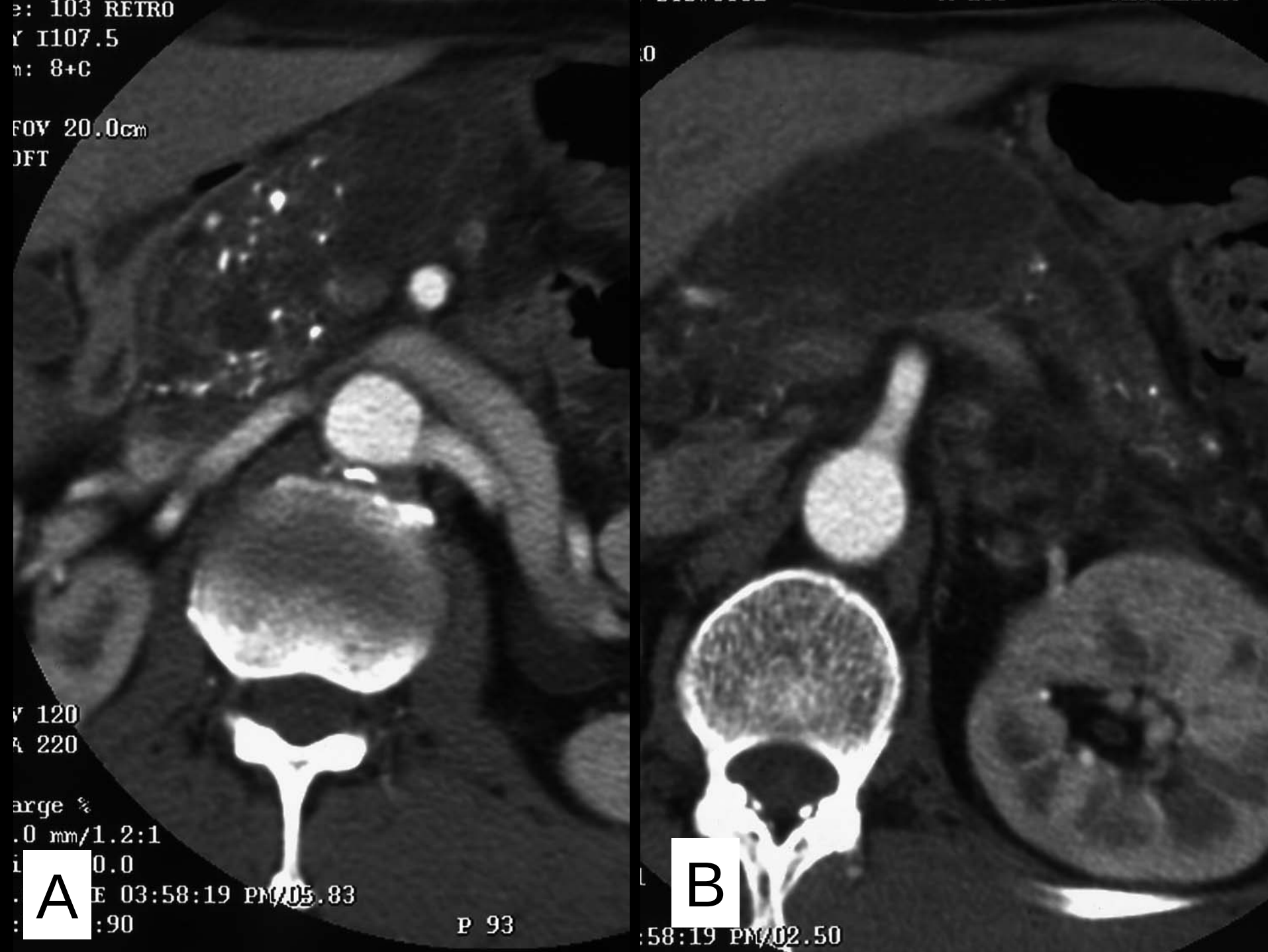
A
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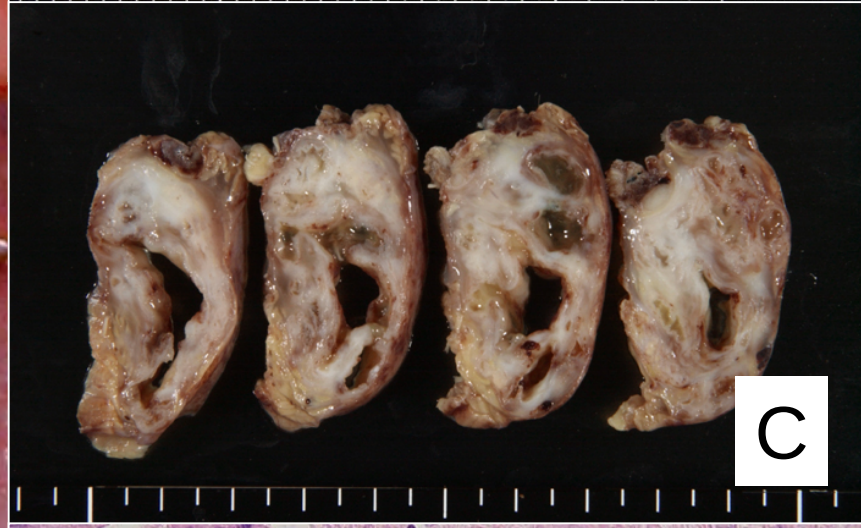
A


B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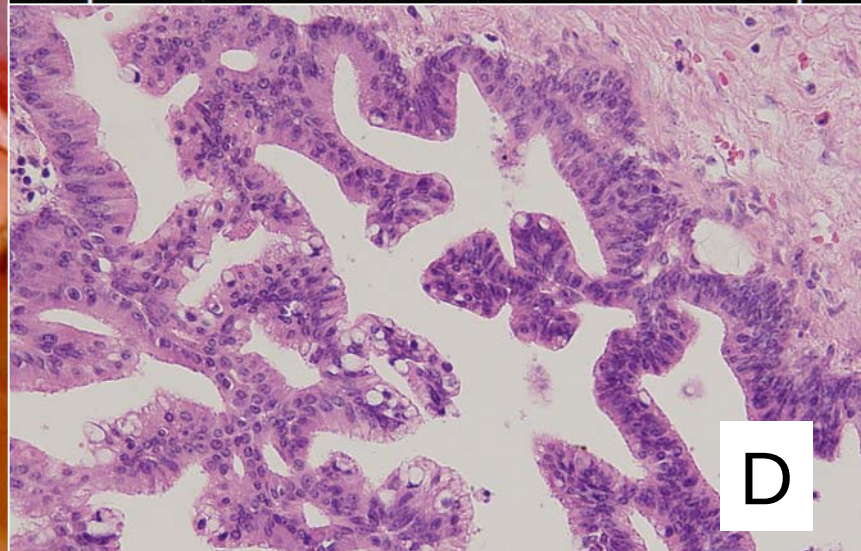
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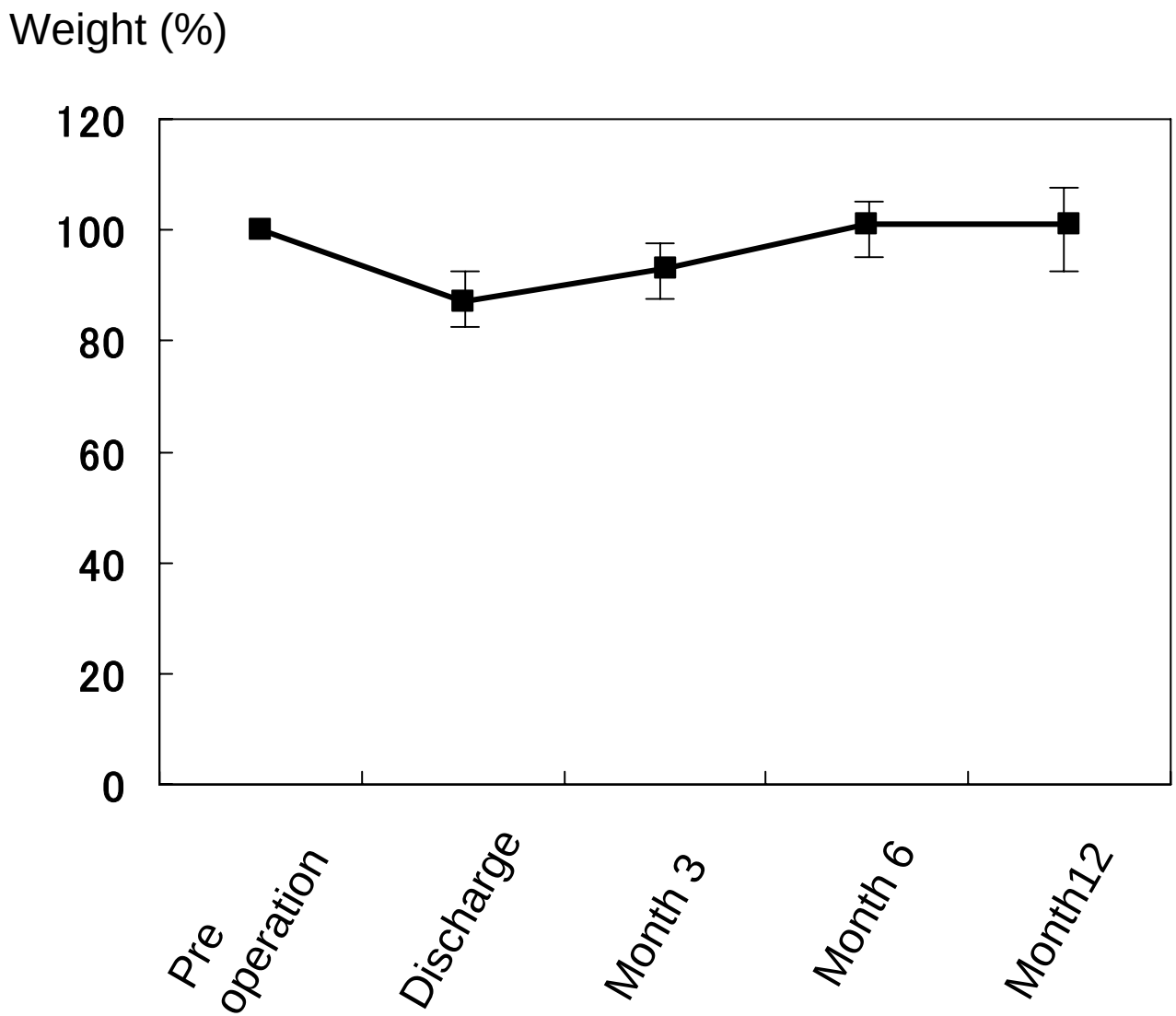
Weight (%)
120
100
80
60
40
20
0
Pre operation
Discharge
Month 3
Month 6
Month12

Table 1 Clinical features of five patients with IPMN that underwent a pylorus-preserving total pancreatectomy

| Patient No | Age (yr)/Sex | Chief complaint | Mucin hypersecretion | CEA (≦5.0 ng/ml) | CA19-9 (≦37 IU/L) | DM | Cytology of pancreatic juice | Type of IPMN |
|---|---|---|---|---|---|---|---|---|
| 1 | 73/ M | Epigastric pain | Yes | 5.2 | 6.1 | Yes | ND | Branch |
| 2 | 74/ F | Epigastric pain | Yes | 2.0 | 28.1 | Yes | negative | Branch |
| 3 | 60/ F | Back pain | Yes | 2.1 | 3.0 | Borderline | negative | MPD |
| 4 | 71/ M | Epigastric pain | Yes | 1.9 | 11.0 | Yes | adenocarcinoma | Branch |
| 5 | 59/ M | None | Yes | 5.9 | 32.0 | Yes | negative | Branch |

yr, year; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; DM, diabetes mellitus; IPMN, Intraductal papillary-mucinous neoplasm; M, male, F, female; ND, not done; MPD, main pancreatic duct

Table 2 Operative findings of the five patients undergoing a pylorus-preserving total pancreatectomy

| Patient No | Indication of PPTP | Operation time (minuets) | Blood loss (g) | Spleen preservation | Final diagnosis | Lymph node metastasis | Surgical margin |
|---|---|---|---|---|---|---|---|
| 1 | Recurrent IPMN | 342 | 1,062 | No | Malignant IPMN (non-invasive) | None | Negative |
| 2 | Recurrent IPMN | 363 | 800 | No | Borderline IPMN | None | Negative |
| 3 | Entire involvement | 390 | 998 | No | Invasive carcinoma derived from IPMN | None | Negative |
| 4 | Recurrent IPMN | 302 | 357 | No | Malignant IPMN (non-invasive) | None | Negative |
| 5 | Entire involvement | 525 | 371 | Yes | Borderline IPMN | None | Negative |

Table 3 Follow-up data of the five patients undergoing a pylorus-preserving total pancreatectomy

| Patient No | Postoperative gastric ulcer | Fatty liver | Diabetic retinopathy | Insulin | Recurrence | Outcome | Follow-up (months) |
|---|---|---|---|---|---|---|---|
| 1 | Yes | No | No | R(10-6-8) | No | Dead due to suicide | 16 |
| 2 | Yes | Yes | Yes | 30R (16-0-8) | No | Alive | 127 |
| 3 | No | Yes | Yes | 30R (26-0-6) | No | Alive | 125 |
| 4 | Yes | Yes | No | 50R (18-8-8) | No | Alive | 75 |
| 5 | No | No | No | 30R (20-0-6) | No | Alive | 62 |