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# Resectable invasive IPMN versus sporadic pancreatic adenocarcinoma of the head of the pancreas: Should these two different diseases receive the same treatment? A matched comparison study of the French Surgical Association (AFC)

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**Abstract**

*Purpose*: To compare survival and impact of adjuvant chemotherapy in patients who underwent pancreaticoduodenectomy (PD) for invasive intraductal papillary mucinous neoplasm (IIPMN) and sporadic pancreatic ductal adenocarcinoma (PDAC).
*Methods*: From 2005 to 2012, 240 patients underwent pancreatectomy for IIPMN and 1327 for PDAC. Exclusion criteria included neoadjuvant treatment, pancreatic resection other than PD, vascular resection, carcinoma *in situ*, or <11 examined lymph nodes. Thus, 82 IIPMN and 506 PDAC were eligible for the present study. Finally, The IIPMN group was matched 1:2 to compose the PDAC group according to TNM disease stage, perineural invasion, lymph node ratio, and margin status.
*Results*: There was no difference in patient's characteristics, intraoperative parameters, postoperative outcomes, and histologic parameters. Overall survival and disease-free survival times were comparable between the 2 groups. In each group, overall survival time was significantly poorer in patients who did not achieve adjuvant chemotherapy ($p = 0.03$ for the IIPMN group; $p = 0.03$ for the PDAC group). In lymph-node negative patients of the IIPMN group, adjuvant chemotherapy did not have any significant impact on overall survival time (OR = 0.57; 95% CI [0.24–1.33]). Considering the whole population (i.e. patients with IIPMN and PDAC; n = 246), patients who did not achieve adjuvant chemotherapy had poorer survival ($p < 0.01$).
*Conclusions*: The courses of IIPMN and PDAC were similar after an optimized stage-to-stage comparison. Adjuvant chemotherapy was efficient in both groups. However, in lymph node negative patients, adjuvant chemotherapy seemed not to have a significant impact.


*Keywords:* Invasive IPMN; Pancreatic adenocarcinoma; Staging; Adjuvant chemotherapy

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## Introduction

In 1996, pancreatic intraductal papillary mucinous neoplasm (IPMN) was defined by the World Health Organization (WHO)[1] as a mucin-producing cystic lesion with pancreatic ductal communication. The disease has variable malignancy potential, graded pathologically by the degree of dysplasia or invasion (low-grade dysplasia, high-grade dysplasia, invasive).[2] It is well established that invasive IPMN (IIPMN) confers a clearly distinct poor prognosis compared with IPMN.[3] However, numerous studies have shown that patients with IIPMN may have better survival compared to patients with sporadic pancreatic ductal adenocarcinoma (PDAC). To address this possibility, recent studies used matched comparisons of these groups,[4,5] with some showing a favorable prognosis for IIPMN compared with PDAC. This led to speculation that the underlying tumor biology differs between them, with a more indolent course for invasive cancer derived from IPMN.[6–8] By contrast, poor outcomes for both diseases have been reported.[9–11] These conflicts might arise from the utilization of nonhomogeneous populations, different pancreatectomy surgical procedures, and, for the matching studies, the omission of histological factors, other than TNM staging,[12] which are known to strongly influence survival. Moreover, patients with IIPMN commonly achieve adjuvant chemotherapy validated for PDAC but the role of adjuvant chemotherapy in patients with resected IIPMN remains unclear particularly in patients with early stage.[13]

The present study aimed to compare survival outcomes and the impact of adjuvant chemotherapy in patients who underwent pancreaticoduodenectomy (PD) for IIPMN and PDAC.

## Methods

### *Patient selection*

From January 1, 2005, to December 31, 2012, 240 consecutive patients underwent a pancreatectomy for IIPMN across 21 French institutions. Standardized clinical data from each institution were entered into a central database: to ensure a uniform interpretation of the retrospective data, 2 experienced pancreatic surgeons reviewed the data prior to database entry. Patients who (a) had >20% of unfilled items on the data form (n = 11), (b) underwent surgery after a period of observation of a diagnosed IPMN (n = 10), (c) underwent neoadjuvant treatment (n = 6), (d) underwent pancreatic resection other than PD (n = 108), (e) required portal vein/superior mesenteric vein or arterial resection (n = 7), (f) had unclear histology or carcinoma *in situ* at the final pathologic examination (n = 7), (g) had <11 examined lymph nodes[14] (n = 7), and (h) had synchronous metastatic disease (n = 2) were excluded. Finally, 82 patients comprised the IIPMN group. Following the same exclusion criteria, 506 patients of 1327 from a multicentric database of the French Association of Surgery who underwent PD for PDAC were used to compose the PDAC group after a matching process (see below).

The database was approved by each center review board, and the final database of IPMN was approved by the French Commission Nationale Informatique et Liberté.

### *Data forms*

Preoperative data included age, sex, jaundice, weight loss, abdominal pain, body mass index (BMI), carbohydrate antigen 19-9 (CA 19-9) serum level, biliary stenting, and an IPMN evaluation according to the Sendaï classification.[15] Intraoperative data included blood loss and surgery duration. Postoperative data included mortality, morbidity,[16] postoperative pancreatic fistula,[17] hemorrhage, reintervention, and length of stay. Histological data included tumor size (measure of the invasive component when IIPMN) and tumor classification according to the TNM classification of the AJCC.[12] Maximal tumor size was recorded as the maximum diameter at pathological analysis. Histological tumor differentiation was defined as well, moderate, or poor. Resection margin status was positive (R1 or R2 resection) or negative (R0 resection). Nodal stage was determined by the number of positive examined lymph nodes, and the lymph node ratio was calculated. Perineural invasion status was also noted. For patients with IIPMN, type (i.e. main duct, branch duct, or mixed) and subtype (pancreatobiliary, gastric, intestinal, and oncocytic) were recorded.

Follow-up data included the achievement of adjuvant chemotherapy, patient status (alive without disease, alive with disease, dead with disease, or dead without disease), and the cause of death (disease recurrence or another cause). Recurrence type was defined as isolated local or metastatic recurrence.

### *Statistical analyses*

The 82 patients comprising the IIPMN group were matched 1:2 with patients from the PDAC group according to disease stage,[12] but also to perineural invasion,[18] lymph node ratio,[19,20] and margin status, as they are recognized as strong independent factors that influence survival after PD for PDAC. Categorical variables are described in terms of frequencies and percentages. The distributions of continuous variables are described as the mean ± the standard error. The statistical associations between the categorical factors were assessed using the Fisher's exact test. Statistical significance was set at $p < 0.05$. Kaplan–Meier overall survival estimates were calculated from the date of surgery and compared using the log-rank test. Disease-free survival was calculated from the time of resection to recurrence:

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