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Intraductal Papillary Mucinous Neoplasms of the Pancreas: Indication, Extent, and Results of Surgery

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Although recognized before the 1980s [1], intraductal and papillary mucinous neoplasm (IPMN) of the pancreas was first described as a distinct entity in 1982 [2] and since then has become an important surgical topic. Today it is fully accepted that IPMN is a precursor of pancreatic adenocarcinoma and involves successive stages of dysplasia, as described in the World Health Organization (WHO) classification of pancreatic neoplasms [3,4]. To date, pancreatic resection before occurrence of invasive carcinoma is the only treatment avoiding the disastrous prognosis of the latter condition. Conversely, long-term prognosis after pancreatic resections for noninvasive IPMN is good, so the indications for pancreatic surgery have increased to prevent adenocarcinoma [5,6]. Even if pancreatic resections are associated with a very low mortality today, they still carry an important morbidity of up to 50% [7–10]. Furthermore, IPMN is observed mainly in the seventh decade, so indications for "preventive" surgery can be difficult to determine, especially in patients carrying a significant surgical risk [5]. IPMN also has emerged as an indication for uncommon techniques of pancreatic resection, including total pancreatectomy and limited resection (enucleation, resection of the ventral pancreas, or medial pancreatectomy) [9,11,12], thus giving the pancreatic surgeon a wider armamentarium than possible for other indications.

The aims of surgery differ according to the presence of malignancy. For malignant IPMN and especially for invasive malignancy, radical resection is essential but entails a substantial operative risk and long-term pancreatic insufficiency. For benign IPMN, in theory, the operative risk and the loss of pancreatic function should be minimal. Thus, surgery for malignant and

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benign IPMN differs in patient selection, surgical technique, and accepted risk of long-term functional disorders. These differences underline the need for (1) a good knowledge of both the pathology and the natural history of the disease; (2) an accurate diagnosis of the disease and its severity, particularly differentiating invasive from noninvasive IPMN (this point is more important in asymptomatic patients in whom IPMN is an incidental finding); and (3) an accurate appreciation of extent of the disease in the pancreatic gland. This article details the indications, surgical techniques, and results of surgery in IPMN.

Pathology and natural history of intraductal and papillary mucinous neoplasms of the pancreas

The WHO classification of pancreatic neoplasms published in 1996 [3] and modified in 2000 [4] reported four successive stages of IPMN: mild dysplasia (IPMN adenoma), moderate dysplasia (border-line IPMN), severe dysplasia (IPMN carcinoma in situ), and invasive carcinoma. Only the last stage of the disease is associated with the adverse prognostic factors identified in ductal adenocarcinoma (poor differentiation, lymph node metastases, lymphatic/vascular embolism, perineural invasion, and peritoneal or hepatic metastases).

Median age at diagnosis ranges from 61 to 68 years [5,6,11,13–24]. In three series [10,16,21] and in one multi-institutional report [25], the median age of patients who had mild or moderate dysplasia was 2 to 6 years younger than that of patients who had carcinoma, but most other series reported no differences in age [6,19,20,23,26,27]. There are no substantial data in the literature to determine how many years are required for benign IPMN to evolve before becoming symptomatic. Because IPMN rarely is diagnosed before the age of 40 years [5,13,14,22,27,28], it probably appears in most patients during the fourth or fifth decade of life.

The risk of malignant transformation depends on the pathologic subtype. In surgical series, the prevalence of malignant transformation (both carcinoma in situ and invasive carcinoma) ranges from 10% to 59% when IPMN is confined to the branch ducts (branch-duct type IPMN) (Fig. 1) and from 56% to 92% when IPMN involves the main duct exclusively (main-duct type IPMN) (Fig. 2) or both the main duct and the branch ducts (mixed-type IPMN) (Fig. 3) (Table 1). One prospective study evaluated the 5-year incidence of carcinoma (both invasive and noninvasive) as 63% for main-duct type and mixed-type IPMN versus 15% for branch-duct type IPMN [13].

It has been suggested recently that IPMN could be a particular subtype of familial pancreatic cancer [37]. Although there are no available data suggesting that relatives of patients who have IPMN should be screened, the relationship between IPMN and familial pancreatic cancer should be clarified in