Impact of Intraoperative Pancreatoscopy with Intraductal Biopsies on Surgical Management of Intraductal Papillary Mucinous Neoplasm of the Pancreas

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BACKGROUND: Because of its known malignant potential, precise histologic diagnosis of intraductal papillary mucinous neoplasm of the pancreas (IPMN) during intraoperative pancreatoscopy (IOP) is essential for complete surgical resection. The impact of IOP on perioperative IPMN patient management was reviewed over 20 years of practice at Cliniques universitaires Saint-Luc, Brussels, Belgium.

STUDY DESIGN: Among 86 IPMN patients treated by pancreatectomy between 1991 and 2013, 21 patients had a dilated main pancreatic duct enabling IOP and were retrospectively reviewed. The IOP was performed using an ultrathin flexible endoscope and biopsy forceps, and specimens of all suspicious lesions underwent frozen section examination.

RESULTS: Complete IOP with intraductal biopsies was easily and safely performed in 21 patients, revealing 8 occult IPMN lesions. In 5 cases (23.8%), initially planned surgical resection was modified secondary to IOP: 3 for carcinoma in situ and 2 for invasive carcinoma. The postoperative morbidity rate at 3 months was 25.0% (5 of 20); 1 patient died from septic shock postoperatively and was excluded. Median follow-up was 93 months (range 13 to 248 months). Nineteen of 21 patients were still alive and free of disease at last follow-up (90.5%); there was 1 patient with invasive carcinoma at initial pathology (pT3 N1) who died of pulmonary recurrence 21 months after surgery.

CONCLUSIONS: Intraoperative pancreatoscopy of the main pancreatic duct combined with intraductal biopsies plays a significant role in the surgical management of IPMN patients and should be used in all patients presenting a sufficiently dilated main pancreatic duct. (J Am Coll Surg 2015;221:982–987. © 2015 by the American College of Surgeons)

Intraductal papillary mucinous neoplasms of the pancreas (IPMNs) are increasingly diagnosed tumors that are often asymptomatic in their first stages and are characterized by papillary proliferations of mucin-producing ductal epithelium, leading to dilatation of the main pancreatic duct or its sub-branches. The overall incidence of IPMN is difficult to assess, but with increased routine use of computed tomography and magnetic resonance imaging, diagnosis of asymptomatic cystic lesions of the pancreas was recently observed to be more than 4%, half of which were neoplastic; IPMN constituted 40% of these, so the incidence of IPMN incidence was about 0.8%.[1] The IPMN spreads longitudinally along the ducts and has a significant potential for malignant transformation, with the presence on biopsy of diffuse or multifocal high grade dysplasia ranging from 7% to 54%.[2-7] Pancreatic IPMNs are classified, based on imaging, into main-duct (MD), branch-duct (BD), or mixed subtypes, depending on the involvement of the ductal system.[8] Prognosis depends on the presence or absence of invasive

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Abbreviations and Acronyms

BD = branch duct
CT = computed tomodensitometry
EUS = endoscopic ultrasonography
IPMN = intraductal papillary mucinous neoplasm
IOP = intraoperative pancreatoscopy
MD = main duct
MRCP = magnetic resonance cholangiopancreatography
POP = peroral pancreatoscopy

carcinoma, reported to occur in around 70% of MD-IPMN.[9]

Preoperative investigations include computed tomodesitometry (CT), ERCP, endoscopic ultrasonography (EUS), and/or magnetic resonance cholangiopancreatography (MRCP). These routine imaging technologies help to distinguish IPMN from other cystic lesions of the pancreas, but cannot reliably differentiate benign from malignant disease. Preoperative peroral pancreatoscopy (POP) is not considered routine imaging because it is technically difficult; however, it does enable direct observation and biopsy sampling of the ductal epithelium. Intraoperative pancreatoscopy (IOP) was first described in 1998 by Kaneko and colleagues, who found the technique safe, effective, and easily performed.[10] There have been only rare reports evaluating the usefulness of IOP for IPMN. Because of the potential malignant growth, complete resection of IPMN lesions is essential and requires precise diagnosis of the extent of the disease. In a previous study, we reported our clinical experience with surgical management of IPMN, highlighting the importance of intraoperative ultrasound, frozen sections of the surgical margins, and perioperative endoscopic examination of the main pancreatic duct with staged biopsies.[11] This study's objective was to report our experience with using IOP with intraductal biopsies for IPMN of the pancreas and the impact of IOP on the perioperative therapeutic decision.

METHODS

From December 1991 to March 2014, 86 consecutive patients with IPMN of the pancreas were treated by surgical pancreatic resection at Cliniques universitaires Saint-Luc, Brussels, Belgium, and were retrospectively reviewed. Operative risk and comorbidities were evaluated according to the American Society of Anesthesiology (ASA) physical score.[12]

Diagnosis of IPMN was based on imaging, endoscopy, and pathologic examination including cytology and histopathology. Preoperative assessment was made by CT, MRCP, and EUS, with histopathologic examination of pancreatic fluid or biopsies of suspicious lesions. Five patients had a preoperative POP.

Indications for surgery were defined according to the International Consensus Guidelines for Management of IPMN in 2006, reporting that all MD tumors should be resected, while only BD tumors > 3 cm, symptoms, and/or high risk stigmata should need a surgical resection (Sendai criteria).[13] For patients treated before 2006, indications for surgery were IPMN with symptoms or suspicion of malignancy.

Only IPMN classified as MD subtype (37 patients) and mixed subtype (33 patients) were considered. The 16 remaining IPMN were of the BD subtype. Selection of patients for IOP was based on the main pancreatic duct diameter within the pancreatic remnant being wider than 5 mm to enable introduction of a flexible endoscope. Among patients with a dilated main pancreatic duct ($n = 70$), IOP could be performed in only 21 patients (30.0%). In the 49 patients not included, 43 had a main pancreatic duct within the pancreatic remnant that was not wide enough, 2 had a total pancreatectomy as planned after preoperative assessment, 3 had a total pancreatectomy after positive frozen sections, and 1 could not support a total pancreatectomy despite positive frozen sections.

At frozen section and final pathology of surgical and intraductal specimens, low and moderate grade dysplasia were considered benign, and high grade dysplasia, carcinoma in situ, and invasive carcinoma were considered malignant; carcinomas were classified according to the WHO classification system.[14] For patients treated before 1996 (before inclusion of the concept of IPMN), pathology was reviewed and reassessed.

Technique

At exploration under laparoscopy ($n = 1$) or laparotomy ($n = 20$), the pancreatic lesion was explored and located precisely, using intraoperative ultrasonography, to define surgical margins. After transection of the pancreas, exploration of the main pancreatic duct was performed on the remaining pancreas with an ultrathin flexible endoscope (external diameter of 3.3 mm or 4.9 mm, Olympus). Pathognomonic lesions of IPMN, such as papillary protrusions, fish-egg–like protrusions, and other atypical lesions, were carefully sought. Biopsy forceps were used through the operative channel to perform intraductal biopsies, which were analyzed by frozen section. Extent of resection was determined by paying careful attention to preoperative investigations, to frozen sections of the surgical margins, and to IOP.