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Surgical management of intraductal papillary mucinous neoplasm with main duct involvement: an international expert survey and case-vignette study

Lianne Scholten[a,1], Nadine C.M. van Huijgevoort[b,1], Marco J. Bruno[c], Carlos Fernandez–del Castillo[d], Sohei Satoi[e], Alain Sauvanet[f], Christopher Wolfgang[g], Paul Fockens[b], Suresh T. Chari[h], Marco Del Chiaro[i], Jeanin E. van Hooft[b,2], Marc G. Besselink[a,2,*], European Study Group on Cystic Tumours of the Pancreas and the International Association of Pancreatology

[a] *Department of Surgery, Cancer Center Amsterdam, Academic Medical Center Amsterdam, the Netherlands*
[b] *Department of Gastroenterology and Hepatology, Amsterdam Gastroenterology and Metabolism, Academic Medical Center Amsterdam, the Netherlands*
[c] *Department of Gastroenterology and Hepatology, Erasmus Medical Center Rotterdam, the Netherlands*
[d] *Department of Surgery, Massachusetts General Hospital, Boston, MA*
[e] *Department of Surgery, Kansai Medical University, Hirakata, Japan*
[f] *Department of Surgery, Beaujon Hospital, Clichy, France*
[g] *Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD*
[h] *Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN*
[i] *Division of Surgery, Departments of Clinical Science, Intervention and Technology (CLINTEC), Karolinska Institute at Karolinska University Hospital, Stockholm, Sweden*

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ABSTRACT

Background: The risk of invasive cancer in resected intraductal papillary mucinous neoplasm with main pancreatic duct involvement is 33%–60%. Most guidelines, therefore, advise resection of main duct intraductal papillary mucinous neoplasm and mixed type intraductal papillary mucinous neoplasm in surgically fit patients, although advice on the surgical strategy (partial or total pancreatectomy) differs. We performed a survey amongst international experts to guide the design of future studies and help to prepare for a single international set of guidelines.

Methods: An online survey including case vignettes was sent to 221 international experts who had published on main duct/mixed type intraductal papillary mucinous neoplasm in the previous decade and to all surgeon and gastroenterologist members of the pancreatic cyst guideline committees of the European Study Group and the International Association of Pancreatology.

Results: Overall, 97 experts (67 surgeons, 30 gastroenterologists) from 19 countries replied (44% response rate). Most (93%) worked in an academic hospital, with a median of 15 years' experience with intraductal papillary mucinous neoplasm treatment. In main duct/mixed type intraductal papillary mucinous neoplasm patients with pancreatic duct dilation (>5 mm) in the entire pancreas, 41% ($n=37$) advised nonoperative surveillance every 3–6 months, whereas 59% ($n=54$) advised operative intervention. Of those who advised operative intervention, 46% ($n=25$) would perform a total pancreatectomy and 31% ($n=17$) pancreatoduodenectomy with follow-up. No structural differences in advice were seen between surgeons and gastroenterologists, between continents where the respondents lived, and based on years of experience.

Conclusion: This international survey identified a clinically relevant lack of consensus in the treatment strategy in main duct/mixed type intraductal papillary mucinous neoplasm among experts. Studies with long-term follow-up including quality of life after partial and total pancreatectomy for main duct/mixed type intraductal papillary mucinous neoplasm are required.

* Corresponding author: Department of Surgery, G4-146-1, Cancer Center Amsterdam, Academic Medical Center, University of Amsterdam, Meibergdreef 9, P.O. Box 22660, 1100 DD Amsterdam, the Netherlands.
E-mail address: m.g.besselink@amc.nl (M.G. Besselink).

[1] Contributed equally
[2] Shared senior authorship

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Table 1
Guidelines IPMN.

	Year	Indication for resection MD-IPMN	Indication for resection MT-IPMN	Suggestion to perform TP
International Association of Pancreatology (IAP)	2017	- Strongly recommended in all surgically fit patients with MPD dilation ≥ 10 mm. - Should be considered in all surgically fit patients with MPD dilation 5-9 mm.	- Strongly recommended in all surgically fit patients with MPD dilation ≥ 10 mm. - Should be considered in all surgically fit patients with MPD dilation 5-9 mm. - Should be considered in all surgically fit patients with a dilated side branch ≥ 30 mm.	- Should be applied selectively in younger patients who can handle the complexities of brittle diabetes and exocrine insufficiency. - Total pancreatectomy should be carefully considered only in patients with a definitive diagnosis and based on the degree of MPD dilation and presence of symptoms or mural nodules. - The threshold for total pancreatectomy should perhaps be lowered in patients with a strong family history of pancreatic ductal adenocarcinoma, because of the increased prevalence of higher-grade lesions.
European study group (EU)	2018	- Strongly recommended in all surgically fit patients with MPD dilation ≥ 10 mm. - Should be considered in all surgically fit patients with MPD dilation 5-9.9 mm.	- Strongly recommended in all surgically fit patients with MPD dilation ≥ 10 mm. - Should be considered in all surgically fit patients with MPD dilation 5-9.9 mm. - Should be considered in all surgically fit patients with a dilated side branch ≥ 40 mm.	- Total pancreatectomy should be considered in patients with entire MPD dilation on imaging with an increased risk for malignancy (i.e. patients with familial pancreatic cancer). - Total pancreatectomy should be considered in patients with entire MDP dilation on imaging with a mural nodule further along the MPD. - If high grade dysplasia or invasive cancer is present at the surgical margin, further resection is warranted, up to a total pancreatectomy.
American Gastroenterological Association (AGA)	2015	- Patients with both a solid component and a dilated pancreatic duct and/or concerning features on EUS (FNA) should undergo surgery to reduce the risk of mortality from carcinoma.	- Patients with both a solid component and a dilated pancreatic duct and/or concerning features on EUS (FNA) should undergo surgery to reduce the risk of mortality from carcinoma.	- Not mentioned.

EUS, endoscopic ultrasonography; *FNA*, fine-needle aspiration; *MD-IPMN*, main duct intraductal papillary mucinous neoplasm; *MPD*, main pancreatic duct; *MT-IPMN*, mixed type intraductal papillary mucinous neoplasm.

Intraductal papillary mucinous neoplasm (IPMN) is a mucin-producing, cystic neoplastic tumor originating from the pancreatic ductal system.[1] IPMN can be subdivided depending on location and extension: main duct (MD)-IPMN, side branch (SB)-IPMN, and mixed type (MT)-IPMN. MD-IPMN is characterized by involvement of the main pancreatic duct, SB-IPMN by involvement of the side branches of the pancreatic duct and MT-IPMN by involvement of both involvement of the main pancreatic duct and its side branches.[2] Although all IPMNs have malignant potential, the risk of high-grade dysplasia or invasive carcinoma is increased if the main duct is involved, with a frequency of invasive carcinoma of 33%–60% in resected specimens.[3-7] Therefore, most guidelines advise resection of MD-IPMN and MT-IPMN in surgically fit patients. The advice on which surgical strategy to follow (eg, partial pancreatectomy with follow-up or total pancreatectomy), however, differs between these guidelines (Table 1).

Those who propose partial pancreatectomy remove only the most involved part of the pancreas, with additional resection suggested when the resection margin is positive for high-grade dysplasia.[8] With this strategy, long-term surveillance of the remnant pancreas is required. The rationale for partial pancreatectomy is to prevent the obligate endocrine and exocrine insufficiency that occurs after total pancreatectomy (TP).[7,9] Because IPMN can be a multifocal disease, it is not unusual that patients develop a recurrence or even malignant disease in the pancreatic remnant after partial pancreatectomy.[10-13] Therefore, others advise total pancreatectomy in patients with MD/MT-IPMN.

The guidelines of the European study group (EU) suggests to consider prophylactic total pancreatectomy only in MD-IPMN when the entire duct is dilated and a mural nodule(s) is present or in patients with familial pancreatic cancer.[7] The American Gastroenterological Association (AGA) does not mention the option of total pancreatectomy.[14] The guidelines of the International Association of Pancreatology (IAP) suggests to consider total pancreatectomy based on the degree of MPD dilatation and presence of nodules or family history of pancreatic cancer in younger patients who can handle the complexities of brittle diabetes and exocrine insuffiency.[9]

To assist the development of a future, single, internationally accepted guideline and to aid the design of prospective studies, we designed this international survey, including detailed case vignettes, regarding the management of IPMN with main duct involvement among experts.

Methods

Survey

Between November 2016 and February 2017, all surgeon and gastroenterologist members of the European Study Group on Cystic Tumours of the Pancreas and the guideline committee on pancreatic cysts of the International Association of Pancreatology and the first and last authors of publications on MD/MT-IPMN in the last 10 years received an email invitation and 3 reminders to participate in an online survey regarding the (surgical) management of MD/MT-IPMN. The survey contained 19 questions on demographics, disease-specific experience, diagnostic approaches, surgical approaches, contraindications for resection, and 6 case vignettes in-

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