

CHINESE MEDICAL SCIENCES JOURNAL

ORIGINAL ARTICLE

Ultrasonographic Characteristics of Intraductal Papillary Mucinous Neoplasm of the Pancreas

Ke Lü, Qing Dai*, Zhong-hui Xu, Yi-xiu Zhang, Li Tan,
Yan Yuan, and Yu-xin Jiang

Department of Ultrasound, Peking Union Medical College Hospital,
Chinese Academy of Medical Sciences & Peking Union
Medical College, Beijing 100730, China

Key words: intraductal papillary mucinous neoplasm; pancreas; ultrasonography

Objective To analyze the clinical and ultrasonographic imaging features of intraductal papillary mucinous neoplasm (IPMN) of the pancreas.

Methods Twelve patients with IPMN underwent surgery between May 2005 and December 2008, including 4 (33.3%) with adenoma and 8 (66.7%) with adenocarcinoma. IPMN was classified preoperatively into 3 types based on sonographic findings of different sites: main duct, branch duct, and combined type. All clinical presentations and ultrasonographic findings of those patients were reviewed and the correlation between ultrasonographic findings and histopathological results was analyzed.

Results There were 9 men and 3 women with a mean age of 60.1 ± 9.6 years (range, 32-73). Of all the 12 patients with IPMN, 9 (75.0%) had experienced some symptoms of epigastric discomfort and/or pain as well as backache; 7 cases were with medical history of acute pancreatitis, 5 cases with diabetes, 4 cases with elevated CA19-9, and 2 cases with steatorrhea. All lesions of IPMN have been revealed by transabdominal ultrasonography. The mean diameters of the lesions were 1.4 ± 0.8 cm (range, 0.5-2.0) and 6.3 ± 6.0 cm (range, 2.0-20.0) in adenomas and adenocarcinomas, respectively. And the mean diameters of the main duct in adenomas and adenocarcinomas were 1.0 ± 0.8 cm and 1.6 ± 1.0 cm, respectively. Among the 4 adenomas, 3 (75.0%) cases were classified as branch type based on sonographic findings, and 2 were demonstrated as mural nodules in which no color signals was detected. Among the 8 adenocarcinomas, 5 (62.5%) cases were classified as main duct type, and 3 (37.5%) as combined type. In 7 of the 8 adenocarcinomas, mural nodules were detected within the dilated ducts or cysts of the lesions in which color flow signals were detected.

Conclusions Transabdominal ultrasonography can reveal the pancreatic cystic lesions of IPMN as well as dilated pancreatic ducts. Some characteristics should be noticed as suggesting the possibility of malignancy: clinical symptoms of pancreatic insufficiency, large tumor size, and mural nodules with color Doppler flow signals. Transabdominal ultrasonography could be a useful tool to help diagnose and make appropriate management of IPMN.

Chin Med Sci J 2010; 25(3):151-155.

INTRADUCTAL papillary mucinous neoplasm (IPMN) of the pancreas is a rare pancreatic tumor. Along with the further understanding of IPMN and the development of medical imaging technology, there were more cases of IPMN reported. However, there were few researches in the diagnostic value of ultrasonography for IPMN. We analyzed the clinical and ultrasonographic imaging features of IPMN of pancreas in order to assess the applicability of transabdominal ultrasonography in diagnosing IPMN.

PATIENTS AND METHODS

Patients

Between May 2005 and December 2008, 12 cases of IPMN undergoing surgery were identified pathologically in Peking Union Medical College Hospital, including 4 (33.3%) adenomas and 8 (66.7%) adenocarcinomas. A retrospective review of clinical and ultrasonographic findings of these cases was conducted.

Transabdominal ultrasonography

Transabdominal ultrasonography was performed with 2-5 MHz curved array transducer using Philips HDI-5000, Philips iU22, and GE LOGIQ9.

The patients fasted for at least 8 hours before the abdominal ultrasonic examinations. Supine position was taken to obtain images of the pancreatic area. Images were saved in the hard disk for further analysis.

Based on the sonographic findings, the lesions of IPMN were classified into 3 types: main duct, branch duct, and combined type. The lesions of IPMN predominantly involving the main pancreatic duct with main duct dilation were classified as main duct type, while lesions mainly involving a branch duct without nodules in the main duct were classified as branch duct type, and those involving both main and branch ducts were classified as combined type.

All clinical presentations and ultrasonographic imaging results were reviewed and the correlation between ultrasonographic findings and histopathological results was analyzed.

Statistical analysis

Continuous variables were expressed as means $\pm$ SD. Statistical analysis was carried out using SPSS 9.0. Descriptive data were reported.

RESULTS

Clinical presentations

There were 9 (75.0%) men and 3 (25.0%) women with a mean age of 60.1 $\pm$ 9.6 years (range, 32-73). Of the 12 patients with IPMN, 9 (75.0%) had experienced symptoms including epigastric discomfort and/or pain and backache, 7 had medical history of acute pancreatitis. Among the 8 malignant cases, 5 presented diabetes and 2 presented steatorrhea. Three (25.0%) cases did not display any symptom and the lesions were found during routine check, among which one lesion was adenoma located in the tail of the pancreas and the other two were adenocarcinomas located in the body and the neck of the pancreas, respectively. Raised serum CA19-9 level was only presented in 4 (33.3%) patients with adenocarcinomas. One patient with malignant IPMN had adenocarcinoma of colon simultaneously. General information and major clinical features of both benign and malignant cases are shown in Table 1.

Ultrasonographic findings

Both dilation of the main pancreatic ducts and lesions of the IPMNs were demonstrated by transabdominal ultrasound. The mean diameter of all the lesions was 4.6 $\pm$ 3.6 cm (range, 0.5-20.0) with dilated main duct of 1.9 $\pm$ 0.8 cm (range, 0.2-3.4). The mean diameter of the lesions in adenomas was 1.4 $\pm$ 0.8 cm (range, 0.5-2.0) with main duct dilation of 1.0 $\pm$ 0.8 cm (range, 0.2-1.9). The mean diameter of the lesions in adenocarcinomas was 6.3 $\pm$ 6.0 cm (range, 2.0-20.0) with main duct dilation of 1.6 $\pm$ 1.0 cm (range, 0.7-3.4).

Six lesions of the IPMN, including 2 adenomas and 4 adenocarcinomas, were demonstrated as multicystic or mixed cystic with solid echogenic components by ultrasound (Figs. 1-3). One adenoma and three adenocarcinomas presented as projecting nodules within the dilated main duct. The other adenoma and an adenocarcinoma were demonstrated as echoic masses located at the head of the pancreas, and the lesion of adenocarcinoma was inhomogenous. Among the 4 adenomas, 3 (75.0%) were classified as branch type, and 1 (25.0%) as main duct type. Among the 8 adenocarcinomas, 5 (62.5%) cases were classified as main duct type, and 3 (37.5%) as combined type. Mural nodules were found within 7 malignant lesions (adenocarcinomas) (7/8, 87.5%), and 5 of them showed abundant color flow signals within the mural nodules (Fig. 3B). On the contrary, mural nodules were found in 2 of the 4 adenomas (2/4, 50.0%) but no color signal was detected within them.

Table 1. General information and major clinical features of both benign and malignant cases of IPMN[§]

Group	n	Age (yr)	Gender (M/F)	Symptomatic (%)	Acute pancreatitis (%)	Diabetes (%)	Steatorrhea (%)	Raised serum CA19-9 level (%)
Adenoma	4	55.8±17.4	3/1	75.0	50.0	0	0	0
Adenocarcinoma	8	62.3± 9.2	6/2	75.0	62.5	62.5	25.0	50.0
Total	12	60.1± 9.6	9/3	75.0	58.3	41.7	16.7	33.3

§: Plus-minus values are means±SD.
IPMN: intraductal papillary mucinous neoplasm.

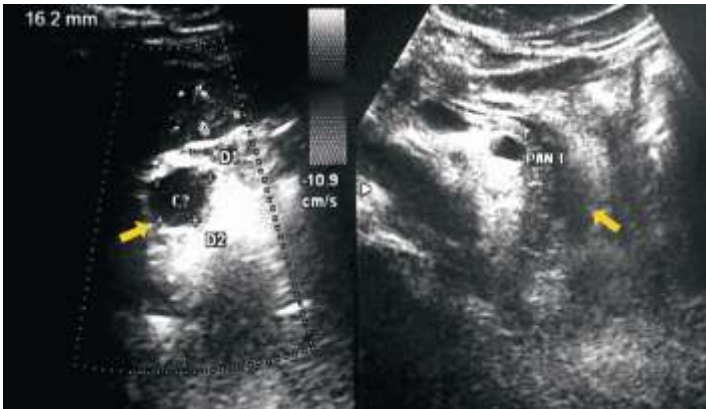


Figure 1. In one case of adenoma, transabdominal ultrasonography shows a cystic lesion (left arrow) and dilated main duct (right arrow). This IPMN, located in the tail of the pancreas and extruding to the pancreatic parenchyma, is classified as branch duct type.



Figure 2. In one case of adenocarcinoma involving the main pancreatic duct, transabdominal ultrasonography shows the obviously dilated pancreatic duct and multiple mural nodules. This IPMN is classified as main duct type.

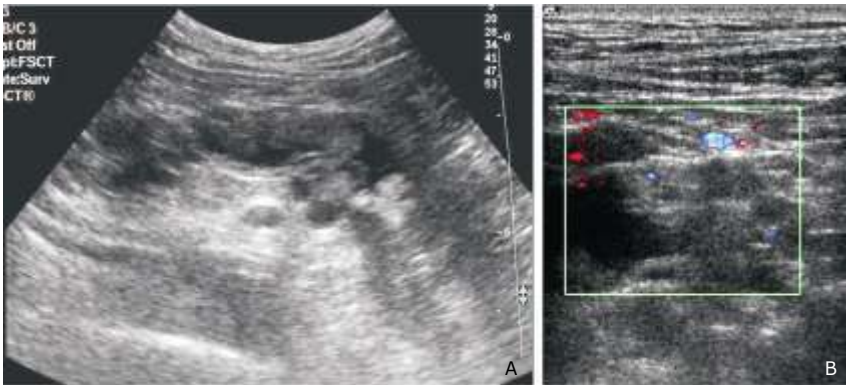


Figure 3. In one case of adenocarcinoma, transabdominal ultrasonography shows obviously dilated pancreatic main and branch ducts (A), and color Doppler reveals the multilocular mixed cystic-solid structure and a few color signals within the mural nodules and walls (B). IPMN in this case is classified as combined type.

DISCUSSION

IPMNs of the pancreas have been defined and classified by the World Health Organization in 1996. IPMNs have malignant potential and undergo transformation from adenoma to borderline neoplasms, followed by carcinoma *in situ* and then invasive carcinoma. Histologically, IPMN displays as neoplastic mucin-producing cells arranged in a papillary pattern. Mucin production by the cells leads to

intraductal mucin accumulation and subsequent cystic dilation of the main or branch ducts.¹ Recently, IPMNs have been increasingly detected. According to the report of Furuta et al,² IPMN accounts for 0.5% of all pancreatic neoplasms diagnosed clinically, and 16.3% of pancreatic neoplasms surgically resected. The distinction between benign and malignant IPMNs has become more important since the complete resection is favorable for improving the prognosis of malignant IPMN and that benign IPMN can be followed up without resection. In this study, we analyzed

the ultrasonographic characteristics of IPMN combined with the clinical presentations in order to further improve the understanding of IPMN, and help diagnose IPMN at the early stage.

In our study, most patients with IPMN were elderly male, with a mean age of 60.1 ± 9.6 years. Moreover, most patients have experienced clinical symptoms. Some of them had symptoms of acute pancreatitis, which may be caused by the partial or complete occlusion of the main pancreatic duct with viscid mucin.³ Persistent occlusion may result in pancreatic insufficiency, which may present as diabetes and steatorrhea. In particular, patients with serious clinical symptoms were all diagnosed histologically as adenocarcinomas in our study. Jaundice may follow the obstruction of bile duct due to the invasion of malignant IPMN although the patients with benign IPMN may also develop obstructive jaundice owing to mucin within the papilla or a fistula extrude into the bile duct.⁴ Serum CA19-9 level was elevated only in malignant IPMN in this study and that in the benign group was all in the normal range. However, some patients with IPMN are asymptomatic, which is probably due to the relatively inactive production of mucin and/or the location of the tumor away from the head of the pancreas.⁵

Although the differences between benign and malignant lesions of IPMN were not of statistical significance in our study, as limited by the case number, the malignant lesions did have bigger size and more dilated pancreatic duct than the benign lesions, half of the IPMN lesions located in the head of the pancreas. Moreover, mural nodules and color flow signal within the nodules were more often detected in the lesions of adenocarcinomas than in those of adenomas. Those findings are consistent with previous reports,^{4,6-12} which consider the main duct $\geq 7-15$ mm, diameter of lesions ≥ 30 mm, and mural nodules within the tumors as predictive factors for malignant IPMNs. However, mural nodules are difficult to demonstrate accurately. It remains difficult to discriminate mucin plugs from mural nodules even in ultrasonography with the intraductal probe.⁵ Itoh et al¹³ pointed out that contrast-enhanced ultrasonography may be helpful for distinguishing benign from malignant lesions. According to that study, the quantitative change in intensity with contrast enhancement is probably a useful parameter for differentiation of benign and malignant IPMNs.

The imaging findings have played a more important role in classifying subtypes of IPMN, which may be helpful for differential diagnosis of IPMN. It was reported that main duct and mixed-type IPMNs are more frequently malignant, while most branch-type IPMNs are benign.⁶ Furthermore, it

is recommended that resection should be done if any of the following five factors are present: a cyst > 3 cm in diameter, mural nodules, dilation of the main pancreatic duct > 6 mm in diameter, positive cytological finding, and symptoms attributable to tumors.¹⁴ However, Nagai et al¹⁵ suggested that the cyst size and number of indications per patient should be taken into account when predicting malignancy of branch duct IPMNs because the specificity of the guidelines for predicting malignancy of those lesions is low.

In our study, the dilated main duct as well as the location and extension of IPMNs were all revealed by transabdominal ultrasonographic imaging, indicating that transabdominal ultrasonography did play an important role in detecting and diagnosing IPMNs. Of all the imaging modalities, transabdominal ultrasonography and CT scan have advantages in demonstrating the entire lesions of IPMNs, but usually fail to depict small cystic tumors of branch ducts as well as mural nodules in less than 10% of patients. However, both ultrasound and CT have lower sensitivity than magnetic resonance cholangiopancreatography and endoscopic ultrasonography do. Endoscopic retrograde cholangiopancreatography failed to detect branch duct ectasia in 12% of patients and occasionally some dilated main ducts because of abundant intraductal or intracystic mucin.⁶ Therefore, combining the findings of multiple methods will be helpful for estimating the characteristics of the lesions.

Differentiating IPMN from other cystic lesions of the pancreas is relatively easy. Radiological imaging of pseudocysts frequently shows a single cystic lesion, with no locular or solid components, and with a wall < 4 mm. Endocrine tumours of the pancreas do not develop cystic areas secondary to pancreatic necrosis presumably because of their better blood supply. Cyst formation is usually unilocular, but may occasionally be microcystic in nature.¹⁶ Notably, it is important to differentiate IPMN from mucinous cystic neoplasm (MCN). Although IPMN and MCN both produce a large amount of mucin, MCN is predominantly found in middle-aged women in the tail of the pancreas, and the tumor appears as a spherical multilocular cyst with a considerably thick, smooth wall and does not show communication with the pancreatic duct.⁵ It has been suggested that ovarian-type stroma is a characteristic histological feature of MCN.

IPMN has been found to be associated with a high incidence (23.6%-32.0%) of malignant non-pancreatic neoplasms.^{5,17} However, this association was not found to be predictive of malignant or invasive IPMN.⁵ We should know that an IPMN may be an indicator of development of non-pancreatic cancers and a thorough examination would be needed for the patients.

In conclusion, IPMN is often found in elderly men and presents with clinical symptoms, especially epigastric discomfort. Cystic or cystic-solid lesions and dilated ducts of the pancreas can be observed by transabdominal ultrasonography. Therefore, transabdominal ultrasonography may be helpful for making diagnosis and appropriate management of IPMN.

REFERENCES

1. Kloeppel G, Solcia E, Longnecker DS, et al. World Health Organization International Histological Classification of Tumours. Histological typing of tumours of the exocrine pancreas. 2nd ed. Berlin: Springer; 1996 .p.1-61.
2. Furuta K, Watanabe H, Ikeda S. Differences between solid and duct-ectatic types of pancreatic ductal carcinomas. *Cancer* 1992; 69:1327-33.
3. Tanaka M. Intraductal papillary mucinous neoplasm of the pancreas diagnosis and treatment. *Pancreas* 2004; 28:282-8.
4. Sugiyama M, Izumisato Y, Abe N, et al. Predictive factors for malignancy in intraductal papillary mucinous tumours of the pancreas. *Br J Surg* 2003; 90:1244-9.
5. Tanaka M, Kobayashi K, Mizumoto K, et al. Clinical aspects of intraductal papillary mucinous neoplasm of the pancreas. *J Gastroenterol* 2005; 40:669-75.
6. Sugiyama M, Atomi Y. Intraductal papillary mucinous tumors of the pancreas: imaging studies and treatment strategies. *Ann Surg* 1998; 228:685-91.
7. Song B, Hu XG, Jin G. Clinical and image features of different pancreatic intraductal papillary mucinous tumors. *J Med Postgrad* 2008; 21:513-6.
8. Fan F, Hu XG, Zhang YJ, et al. Clinical and radiological characteristics of benign and malignant intraductal papillary mucinous tumors of the pancreas. *Ti Erh Chun i Ta Hsueh Hsueh Pao* 2008; 29:193-6.
9. Murakami Y, Uemura K, Hayashidani Y, et al. Predictive factors of malignant or invasive intraductal papillary mucinous neoplasms of the pancreas. *J Gastrointest Surg* 2007; 11:338-44.
10. Taouli B, Vilgrain V, Vullierme MP, et al. Intraductal papillary mucinous tumors of the pancreas: helical CT with histopathologic correlation. *Radiology* 2000; 217:757-64.
11. Jang JY, Kim SW, Ahn YJ, et al. Multicenter analysis of clinicopathologic features of intraductal papillary mucinous tumor of the pancreas: is it possible to predict the malignancy before surgery? *Ann Surg Oncol* 2005; 12: 124-32.
12. Irie H, Honda H, Aibe H, et al. MR cholangiopancreatographic differentiation of benign and malignant intraductal mucin producing tumors of the pancreas. *AJR* 2000; 174:1403-8.
13. Itoh T, Hirroka Y, Ttoh A, et al. Usefulness of contrast-enhanced transabdominal ultrasonography in the diagnosis of intraductal papillary mucinous tumors of the pancreas. *Am J Gastroenterol* 2005; 100:144-52.
14. Tanaka M, Chari S, Adsay V, et al. International consensus guidelines for management of intraductal papillary mucinous neoplasms and mucinous cystic neoplasms of the pancreas. *Pancreatol* 2006; 6:17-32.
15. Nagai K, Doi R, Ito T, et al. Single-institution validation of the international consensus guidelines for treatment of branch duct intraductal papillary mucinous neoplasms of the pancreas. *J Hepatobiliary Pancreat Surg* 2009; 16: 353-8.
16. Garcea G, Ong SL, Rajesh A, et al. Cystic lesions of the pancreas. *Pancreatol* 2008; 8:236-51.
17. Sugiyama M, Atomi Y. Extrapaneatic neoplasms occur with unusual frequency in patients with intraductal papillary mucinous tumors of the pancreas. *Am J Gastroenterol* 1999; 94:470-3.