Utility of Multidetector Row CT in Diagnosing Branch Duct IPMNs of the Pancreas Compared with MR Cholangiopancreatography and Endoscopic Ultrasonography

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Received 25 May 2010, accepted 1 September 2010

Edited by MINORU YAGI

Summary: This study aimed to compare the usefulness of multidetector row CT (MDCT), MR cholangiopancreatography (MRCP), and endoscopic ultrasonography (EUS) in diagnosing branch duct intraductal papillary mucinous neoplasms (IPMNs) of the pancreas. Imaging and pathological findings were retrospectively evaluated for 25 patients with branch duct IPMNs of the pancreas who underwent surgical resection (13 adenomas, 4 borderline lesions, and 8 carcinomas). MDCT and MRCP were performed on all 25 patients, whereas EUS was performed on 22 patients. MDCT and MRCP were used to identify features predictive of malignancy, including carcinoma, borderline lesions, and the presence of thickened irregular walls/septa or a solid mass. EUS was used to identify the presence of intramural nodules or a solid mass. Correlations between histopathology and maximum diameter of the main pancreatic duct (MPD) or cyst size detected by MDCT and MRCP were also examined. Presence of a solid mass was highly correlated with malignancy with all imaging methods (MDCT; $P=0.001$, MRCP; $P=0.008$, EUS; $P<0.001$, respectively). Presence of thickened irregular walls/septa on MDCT correlated well with malignancy ($P=0.019$). In contrast, presence of thickened irregular walls/septa on MRCP and intramural nodules on EUS did not correlate with malignancy. No significant correlation was found between malignancy and average maximum MPD diameter or cyst size ($P>0.05$), though values tended to be larger in malignant tumors. Our results suggest that the presence of thickened irregular walls/septa or a solid mass on MDCT are highly correlated with malignancy, and that MDCT is useful for diagnosis of branch duct IPMNs of the pancreas.

Key words intraductal papillary mucinous neoplasms (IPMNs) of the pancreas, multidetector row computed tomography (MDCT), magnetic resonance cholangiopancreatography (MRCP), endoscopic ultrasonography (EUS)

INTRODUCTION

Itraductal papillary mucinous neoplasms (IPMNs) of the pancreas are characterized by massive production and retention of mucin in the pancreatic duct and interstitium, dilation of the papilla of Vater caused by


Original Contribution

Kurume Medical Journal, 57, 91-100, 2010

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Abbreviations: CPR, curved planar reformatting; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasonography; HU, hounsfield units; IPMNs, intraductal papillary mucinous neoplasms; kVp, kilovolts; mAs, milliampere seconds; MDCT, multidetector row CT; MIP, maximum intensity projection; MPD, main pancreatic duct; MPR, multiplanar reformatting; MRCP, magnetic resonance cholangiopancreatography; RARE, rapid acquisition with relaxation enhancement; 3D-TSE, three-dimensional turbo spin echo; WHO, World Health Organization.
mucinous flow, little tendency for infiltration, and good prognosis [1]. Pathologically, IPMNs can manifest with different degrees of cellular atypia, ranging from hyperplasia, to adenoma with varying degrees of dysplasia or invasive carcinoma. IPMNs can be classified as either main duct IPMNs or branch duct IPMNs based on imaging studies [2,3]. Main pancreatic duct types are indicated for surgery regardless of the presence of intramural nodules; cyst diameter, main pancreatic duct diameter, and the presence of intramural nodules are considered important findings for branch duct types. However, the intramural nodule size diagnostic of malignancy and diagnostic testing methods for branch duct types vary among reports, and currently are not uniform.

Many imaging techniques can be used to evaluate branch duct IPMNs of the pancreas, including CT, magnetic resonance cholangiopancreatography (MRCP), endoscopic retrograde cholangiopancreatography (ERCP), and endoscopic ultrasonography (EUS). MRCP is currently being investigated as the preferred imaging modality for diagnosis and follow-up of branch duct IPMNs of the pancreas [4,5]. CT remains the most commonly used imaging method, as well as the initial method of choice for evaluating patients with pancreatic disease. Multidetector row CT (MDCT) involves the use of very thin collimation for the acquisition of high-resolution images during multiple phases of contrast enhancement, resulting in enhanced evaluation of the communication between the main pancreatic duct (MPD) and cystic lesion, and simultaneous evaluation of the pancreatic parenchyma and pancreatic duct [6]. The purpose of this study was to compare the predictive features of malignancy identified by MDCT, MRCP, and EUS in branch duct IPMNs of the pancreas, as well as to examine the correlations between histopathology and maximum MPD diameter or cyst size detected by MDCT and MRCP.

MATERIALS AND METHODS

Patients

Forty-five (45) patients at our institution were diagnosed with branch duct IPMNs of the pancreas based on ERCP findings between August 2003 and December 2008. Of the 45 patients, 25 underwent surgical resection without follow-up, and the diagnosis of IPMNs of the pancreas was confirmed by pathologic specimen in all cases. The remaining 20 patients were selected for follow-up due to age, poor general condition, or refusal to undergo a surgical procedure. Thus, our study population included 25 patients (20 men and 5 women; average age, 65.2 years; age range, 37-84 years). MDCT and MRCP were performed on all 25 patients. EUS was performed on 22 patients; 3 of the 25 patients refused EUS. Informed consent for participation in the study was obtained from each patient or guardian as part of the protocol approved by the institutional clinical subpanel on human studies at our university hospital.

MDCT technique

Contrast-enhanced dynamic CT scans (unenhanced, arterial, pancreatic parenchymal, portal, and delay phases) were performed with a 16-detector row scanner (Light Speed Ultra; GE Healthcare, Milwaukee, WI, USA). All patients fasted for at least 5 hrs prior to examination and received 100 mL of nonionic contrast material (Iopamidol, 370 mgI/mL; Bayer Schering Pharma, Berlin, Germany) intravenously by means of a power injector (Auto Enhance A-50; Nemoto-Kyorin-Dou, Tokyo, Japan) at a rate of 4 mL/s. Scans were acquired in the craniocaudal direction with the following parameters: pitch of 1.375:1, 0.7-sec scanning time per rotation, table speed of 13.75-27.50 mm/rotation, and detector configuration of 0.625-1.25×16 mm. Peak tube voltage was 120 kilovolts (kVp), and the current-time product was 300-440 milliamperc seconds (mAs). Using a bolus-triggered technique (SmartPrep; GE Healthcare) in which the cursor was placed on the aorta and the threshold set at 200 Hounsfield units (HU), the arterial, pancreatic parenchymal, portal, and delay phases were initiated at 5, 20, 40, and 70 seconds, respectively, after the trigger threshold was achieved.

CT data for each phase were retrospectively reconstructed with a 0.625 to 1.25 mm section thickness at an interval of 0.625 to 1.25 mm. The raw data were transferred automatically via Ethernet to a workstation (ADW 4.2; GE Medical Systems) in a 512×512-pixel format. The oblique angles for the multiplanar reformatting (MPR) images were selected to follow the course of the main pancreatic duct near the cystic lesion on the axial images. The use of interactive oblique views facilitated selection of the appropriate angles. To generate curved planar reformatting (CPR) images, the operator designated a curved line along the long axis of the pancreas by scrolling and reviewing a stack of axial images. Multiple images were generated parallel to this curved plane.

MRCP technique

MR imaging of the pancreas and MRCP were performed with a 1.5-T system (MAGNETOM Sym-
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phony Maestro Class; Siemens, Erlangen, Germany) using a phased-array body coil. T1-weighted gradient-recalled echo images were obtained through the pancreas before and after fat saturation (repetition time msec/echo time msec, 180/2.1; flip angle, 80°; number of signals acquired, 1; matrix, 192×256; section thickness, 7.00 mm). T2-weighted MRCP was performed using a single-shot rapid acquisition with relaxation enhancement (RARE) and three-dimensional turbo spin echo (3D-TSE) sequence (TR=1590 msec, TE=761 msec) with 1.8-mm section thickness, resulting in a total of 61 sections. All images were post-processed using both maximum intensity projection (MIP) and MPR techniques, including coronal, coronal oblique, and transverse planes. No intravenous contrast material was administered for MRCP.

EUS technique

Endoscopes with 7.5-12-MHz probe radial sector scan transducers (GF-UMQ-200; Olympus, Tokyo, Japan) were used. The echo probe was routinely covered with a water-filled balloon to allow adequate transmission of ultrasound and to improve image quality. The echo endoscope was introduced into the stomach and advanced into the second portion of the duodenum. Tumors were scanned with a water-filled balloon to assess tumor features.

Image analysis

MDCT and MRCP imaging findings were evaluated by the consensus of two radiologists who had 13 and 25 years of experience reading abdominal images, respectively. The readers were aware of the diagnosis of branch duct IPMNs of the pancreas but were blinded to the histopathologic findings. In addition, EUS reports from gastroenterologists were analyzed retrospectively.

Imaging criteria for diagnosing malignancy

Malignancy was diagnosed by MDCT or MRCP when at least one of the following was detected: thickened irregular walls/septa in which enhancement can be demonstrated, or a solid mass within the dilated branch pancreatic duct. A small intramural nodule measuring less than 10 mm associated with enhancing soft-tissue components adjacent to the walls/septa was defined as thickened irregular walls/septa (Fig. 1A). On the other hand, a large intramural nodule measuring 10 mm or larger, and associated with enhancing soft-tissue components adjacent to the wall or septa, was defined as a solid mass (Fig. 1B). Findings of solid mass and thickened irregular walls/septa were evaluated with portal or venous phase axial images, interactive MPR, and source images. Additionally, the maximum diameter of MPD and cyst size were recorded for each patient. The maximum diameters of the MPD and cyst size were measured on the MPR or CPR image and the MIP image. The diameter and size of nodules were measured at the workstation with electronic calipers. Malignancy was diagnosed when

Fig. 1. Schematic diagrams of cystic lesions on MDCT and MRCP.
A. “Thickened irregular walls/septa” were defined as a wall or septum with adjacent enhancing soft-tissue components.
B. “A solid mass” was defined as an intramural nodule measuring 10 mm or larger in the cystic lesion.
either an intramural nodule or solid mass was detected using EUS. Intramural nodules detected by EUS were defined as hyperechoic nodules lining the walls.

**Histopathologic analysis**

A gastrointestinal pathologist with more than 8 years of experience reviewed each pathologic specimen. Tumors were classified into three histologic subtypes by microscopy as follows: adenoma, borderline lesion, or carcinoma. Carcinoma in situ and invasive carcinoma were grouped together as carcinoma. Classifications were made in accordance with World Health Organization (WHO) definitions [7].

**Statistical analysis**

The Bonferroni multiple comparison test was used to assess correlations between continuous variables, including the diameter of the main pancreatic duct and the lesion size. Differences between ordinal variables were evaluated using the Wilcoxon-Mann-Whitney test. A p-value of less than 0.05 was considered statistically significant. Statistical analysis was performed with SPSS for Windows release 12.0.0 (SPSS, Chicago, IL, USA).

**RESULTS**

**Surgical results**

Lesions were resected by pancreaticoduodenectomy in 7 patients, pylorus-preserving pancreaticoduodenectomy in 9 patients, distal pancreatectomy and splenectomy in 6 patients, partial resection in 2 pa-

![Image of a 47-year-old man with intraductal papillary mucinous neoplasm (IPMN) with invasive carcinoma.](image)

**Fig. 2.** A 47-year-old man with intraductal papillary mucinous neoplasm (IPMN) with invasive carcinoma.

A. Curved planar reformation demonstrates a heterogeneous hypoattenuating solid mass measuring 30 mm in diameter in the dilated branch duct (arrow) of the pancreatic body. The main pancreatic duct is diffusely dilated.

B. Source MRCP image shows a solid mass (arrow) in the multilocular cystic lesion.

C. EUS shows a solid mass within a cystically dilated branch duct.

D. Photograph of the resected specimen shows a solid mass in the cystically dilated branch duct. Microscopic examination reveals intraductal papillary adenocarcinoma. The papillary adenocarcinoma spread through the periductal tissue into the pancreatic body.
TABLE 1.
Correlation between presence of thickened walls/septa or solid mass and histology on MDCT

<table>
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<tr>
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<td>absence</td>
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Data are numbers of patients.

![A](image1.png) ![B](image2.png) ![C](image3.png) ![D](image4.png)

**Fig. 3.** A 78-year-old man with intraductal papillary mucinous neoplasm (IPMN) with minimally invasive carcinoma.
A. Axial CT image shows a cystic tumor measuring 45 mm in diameter with thickened irregular walls/septa in the pancreas head.
B. MRCP image shows multiseptated cystic mass with upstream diffuse dilatation of the main pancreatic duct. The cystic mass had low signal intensity septa within the lesion, but did not show thickened irregular septa.
C. EUS shows an intramural nodule as a hyperechoic lesion measuring 8 mm in diameter within the cystic mass.
D. Microscopic examination reveals intraductal papillary adenocarcinoma of the tall columnar epithelium with severe atypia in the pancreatic duct. This figure is reproduced from Reference 6 (Arikawa et al.) with permission from the journal.
patients, and total pancreatectomy in 1 patient.

Pathologic results

Diagnosis of branch duct type IPMN was confirmed by histologic examination and classified as follows: 13 samples (52%) as adenoma, 8 samples (32%) as carcinoma, and 4 samples (16%) as borderline. Of the 8 patients with carcinoma, 5 patients were diagnosed with invasive carcinoma and 3 patients were diagnosed with small or microscopic foci of invasive carcinoma.

Imaging examinations

MDCT and MRCP imaging were performed on all patients without complications. EUS was performed in 19 patients; EUS was unsuccessful in 3 patients because of previous distal gastrectomy with Billroth II anastomosis.

Correlation between histopathology and imaging findings on MDCT

A solid mass was detected in 5 of 8 carcinomas (Figs. 2A, D), but not in adenomas or borderline lesions. Thickened irregular walls/septa were detected by MDCT in 3 of 8 carcinomas (Figs. 3A, D) and in 3 of 4 borderline lesions, but were not detected in adenomas (Figs. 4A, B, D). A significant correlation was found between these MDCT features and malignancy (Table 1).

Correlation between histopathology and imaging findings on MRCP

A solid mass was detected in 5 of 8 carcinomas (Fig. 2B), in none of the borderline lesions, and in 1 of 13 adenomas—although this case was determined to be a false positive (i.e., pancreatic calcification). Thickened irregular walls/septa were detected in 1 of 8 car-

![Fig. 4](image-url)

A 67-year-old man with intraductal papillary mucinous neoplasm (IPMN) with adenoma. A. Curved planar reformation and B. axial contrast enhanced CT image shows the cystic lesion measuring 22 mm in diameter with thin septa in the pancreatic body. The main pancreatic duct is minimally dilated. C. MRCP image shows multiseptated cystic mass with thin septa. D. Microscopic examination reveals the presence of papillae with low-grade dysplasia of the epithelium. The tumor was diagnosed as intraductal papillary adenoma with mild dysplasia.
cinomas (Fig. 3B) and in 1 of 4 borderline lesions, but were not detected in adenomas (Fig. 4C). A significant correlation was found between MRCP detection of a solid mass and malignancy, but no significant correlation was found between the detection of thickened irregular walls or septa and malignancy (Table 2).

**Correlation between histopathology and imaging findings on EUS**

A solid mass was found in 4 of 6 carcinomas (Fig. 2C), in 1 of 3 borderline lesions, but not in adenomas. An intramural nodule was detected in 5 of 10 adenomas, but in none of the 3 borderline lesions, and 1 of 6 carcinomas (Fig. 3C). A significant correlation was found between EUS detection of a solid mass and malignancy, but no significant correlation was found between the detection of an intramural nodule and malignancy (Table 3).

**Correlation between histopathology and the maximum diameter of the MPD or cyst size**

The relationship between histopathologic findings and the mean maximum diameter of the MPD detected by MDCT and MRCP was examined. The mean maximum diameter of MPD for adenoma, borderline lesion, and carcinoma was 6.2±4.9 mm, 6.2±1.5 mm, and 6.6±3.5 mm by MDCT, respectively; and 6.5±1.9 mm, 6.7±3.6 mm, and 6.8±5.5 mm by MRCP, respectively. The values for malignant tumors tended to be larger, but no significant correlation was found between the average maximum diameter of the MPD and malignancy.

The relationship between histopathologic findings and cyst size detected by MDCT and MRCP was also examined. The mean size of adenoma, borderline lesion, carcinoma was 29.0±10.6 mm, 31.9±7.5 mm, and 42.5±21.1 mm by MDCT, respectively; and 29.7±10.6 mm, 31.3±8.5 mm, and 42.2±20.7 mm by MRCP, respectively. The values for malignancy tumors tended to be larger, but no significant correlation was found between cyst size and malignancy.

**DISCUSSION**

Several imaging criteria for branch duct IPMNs of the pancreas have been reported to differentiate malignant lesions from benign lesions. However, the diagnostic significance of these criteria and diagnosis methods have not been established and are controversial. Recently, international guidelines for the management of IPMNs were proposed by the International Association of Pancreatology [8]. These guidelines...
recommend that presence of intramural nodules, cyst size \( >30 \) mm, and dilation of the MPD \( (>6 \) mm) be used as indications for resection. Moreover, the guidelines recommend using MDCT or MRCP to assess the size of the lesion and the MPD diameter. In addition, the guidelines recommend EUS for intramural nodules. EUS may be the most sensitive method for visualizing small architectural features like intramural nodules \([9,10]\); however, this technique has some drawbacks. EUS is an invasive procedure, dependent on technical skills of the operator, and does not provide the surgeon with a visual “road map” to reference for preoperative planning. Thus, minimally invasive or noninvasive imaging methods for diagnostic and preoperative examinations would be advantageous for patients and surgeons. Fukukura et al. \([11]\) reported that papillary proliferation \((\geq3 \) mm) was detected equally well by helical CT and MRCP. However, in our experience, the CT and MRCP techniques often detect only a thickened septum and have difficulty detecting intramural nodules due to the limited spatial resolution of the typically small, flat tumor. Therefore, we compared the ability of the following imaging criteria to diagnose malignancy of branch duct IPMNs: detection of an intramural nodule \((<10 \) mm diameter) or a solid mass \((\geq10 \) mm diameter) by EUS, and detection of a solid mass or thickened irregular walls/septa by MDCT or MRCP.

In our study, the presence of a solid mass correlated well with malignancy for all imaging methods. Previous studies have reported that the presence of a solid mass is predictive of malignancy using several types of imaging, including CT \([12-14]\), MRI \([15]\), and EUS \([9,16]\). Our findings support these studies. We did not see differences in detection rate based on different modalities. In addition, the presence of thickened irregular walls/septa on MDCT also correlated well with malignancy. Procacci et al. \([17]\) reported that in malignant lesions, the wall and septa appear irregular and thick, indicating intramural nodules, whereas both the wall and septa are regular and thin in benign lesions. Carbognin et al. \([18]\) reported that the presence of a thick wall by CT and MR imaging is strongly suggestive of malignancy. In the present study, however, the presence of thickened irregular walls/septa on MRCP did not correlate well with the presence of malignancy. Neither MRCP nor MDCT can visualize fine structures of cystic lesions due to limited spatial resolution. Pathologically, thickened irregular walls/septa mainly result from fibrosis of pancreatic parenchyma due to obstructive chronic pancreatitis and large papillary protrusions lining the dilated branch duct wall. Thus, it is prudent to suspect malignancy when MDCT, but not MRCP, detects thickened irregular walls/septa in which enhancement can be demonstrated. Conversely, MDCT and MRCP detection of hairline-thin septa, or minimal but smooth thickening of walls/septa, suggests benign lesions. The presence of intramural nodules on EUS did not correlate well with malignancy. Kobayashi et al. \([16]\) reported that none of the patients with intramural nodules less than 10 mm visualized by EUS had developed invasive carcinoma at resection. Loftus et al. \([19]\) reported that histologic diagnosis of malignancy depends on the nuclear appearance of the intramural nodule, rather than its presence alone. The presence and size of intramural nodules have previously been considered significant findings in diagnosing malignancy. However, in the present study, nodules less than 10 mm were visualized by EUS in 50\% \((5/10)\) of adenomas, and were not significantly different. In contrast, the presence of thickened irregular walls/septa was not detected in any adenoma by MDCT or MRCP. In MDCT, this finding was observed significantly in malignancies and borderline malignancies. These results suggest that evaluating the presence of thickened irregular walls/septa by MDCT, as well as the presence of intramural nodules, is important in diagnosing malignancy.

Large tumor size and marked dilation of the MPD in branch duct IPMNs have also been reported to be associated with malignancy\([14,20-25]\), but this conclusion was not confirmed by other studies \([4,18,24,26-28]\). In the present study, both maximal MPD diameter and size of the entire cystic lesion were larger in malignant than in benign lesions, but this difference was not statistically significant. This is due to the massive production of mucin characteristic of pancreatic IPMNs, which leads to increased cyst size and a dilated MPD. Thus, increased cyst size and dilated MPD were not necessarily suggestive of malignancy.

There are several limitations to our study. First, it is limited by the small patient sample size; however, all cases were well documented with detailed surgical and pathological findings. Second, while decisions on MDCT and MRCP findings were based on the consensus of two radiologists, we did not evaluate interobserver agreement. Third, criteria for determining malignancy were not the same for all imaging methods. Thickened irregular walls/septa were not evaluated by EUS because this finding was not included in past EUS reports, which were analyzed retrospectively in the present study. Fourth, due to the small sample size and limited number of findings examined, we did not
determine using multivariable analysis whether or not the presence of a solid mass or thickened irregular walls/septa on MDCT is an independent risk factor.

In conclusion, MDCT was useful for diagnosis of branch duct IPMNs of the pancreas. In particular, the presence of a solid mass and thickened irregular walls/septa on MDCT, but not on MRCP or EUS, correlated well with malignancy.

REFERENCES


