Original Article

Ningen Dock International 2020 ; 7 : 14–18

Importance of Magnetic Resonance Cholangiopancreatography in Diagnosis and Follow-up of Intraductal Papillary Mucinous Neoplasms

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Abstract

Objective: We retrospectively compared the ability of abdominal ultrasound (US) and magnetic resonance cholangiopancreatography (MRCP) to depict intraductal papillary mucinous neoplasms (IPMN), which can be precursors of pancreatic cancer.

Methods: In 170 patients with IPMN, lesion detection by US was examined according to site and size of cysts. Additionally, clinical and imaging features associated with need for surgery during follow-up were determined.

Results: Relative to lesion depiction with MRCP as the standard, cyst detection by US was significantly better in the body of the pancreas than in the head or tail. For small cysts (< 10 mm), US detection was significantly better in the body than in the tail. Among 170 patients, 12 (7.1%) underwent surgical resection during follow-up. A widening main pancreatic duct (MPD; diameter increase ≥ 0.2 mm/year) and greater age (≥ 70 years) were significantly and independently associated with need for surgical resection.

Conclusion: The ability of US to detect cysts in the head and tail of the pancreas is limited, particularly in the latter. Since multiple cysts are relatively frequent in these regions, MRCP should also be performed when a cyst is detected in the body by US. Older individuals and those with relatively rapid widening of the MPD should be considered carefully for surgical resection.

Keywords intraductal papillary mucinous neoplasm (IPMN), magnetic resonance cholangiopancreatography (MRCP), abdominal ultrasound (US)

Intraductal papillary mucinous neoplasms (IPMN) are gaining interest as a risk factor for pancreatic cancer. As many patients with branch-duct IPMN tend to be asymptomatic, cysts representing IPMN are often detected incidentally during abdominal ultrasound (US) performed as part of a routine health check-up or in screening for other diseases. Previous studies have reported 5- and 10-year incidence rates for pancreatic cancer during follow-up of IPMN of 3.0% and 8.8%, respectively[1]. However, factors predicting need for surgical resection in patients with IPMN require further clarification. Through early diagnosis of IPMN and careful follow-up, the need for timely pancreatic surgery can be determined, thereby improving outcomes in pancreatic cancer.

A previous comparison of US and computed tomography (CT) in the diagnosis of IPMN showed that US had significantly higher sensitivity[2]. However, diagnosis requires assessment of the communication between a cystically dilated pancreatic branch duct and the main pancreatic duct (MPD), which is often difficult by US. Magnetic resonance cholangiopancreatography (MRCP) is considered superior to US in this respect, but few studies have compared US and MRCP for diagnosis of IPMN.

This retrospective study compared the abilities of US and MRCP to depict IPMN and sought to identify factors associated with eventual need for surgical resection of IPMN.

Materials and Methods

Patients

Our subjects were 170 follow-up patients with branch duct or mixed-type IPMN who had visited our hospital between January 2007 and December 2016. The definition of IPMN was pancreatic cysts communicating with

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the MPD in MRCP. Follow-up patients were defined as those who underwent MRCP on at least 2 occasions at intervals of at least 6 months. Among them, 85 were male and 85 were female and the mean age at diagnosis was 66 ± 11 years (see statistical analysis section). The mean observation period was 30 ± 19 months. All MR examinations were performed using the same devices. The study was approved by the Institutional Review Board of Fujita Health University and conducted in accordance with the ethical principles of the Declaration of Helsinki. Written informed consent was obtained from all patients at the time of MRCP.

Clinical features of IPMN

Clinical and imaging features of IPMN considered in this study included diagnostic modality first detecting a lesion, cyst site(s) within the pancreas (head, body, and/or tail), type of cysts (unilocular or multilocular), mode of cyst onset (single or multiple cysts at onset), mean cyst size by site, and increase in diameter of the MPD.

Ability of US to depict IPMN relative to MRCP

Depiction ability was compared between US and MRCP for IPMN that had been depicted by MRCP. Cysts depicted by US were analyzed by site and size.

Surgical resection for IPMN

Clinical features as well as US and MRCP findings were examined for patients who underwent surgical resection. The clinical features included age, gender, duration of follow-up, single vs. multiple lesions at onset, unilocular vs. multilocular cysts, cyst site, cyst growth rate, rate of MPD diameter enlargement, presence of mural nodules, and presence of masses. Comparisons between malignant and non-malignant cases included the features considered in identifying patients who required surgical resection during follow-up. Annual rates of increase in cyst or MPD diameter were calculated by dividing the observed difference in diameter of the cyst or MPD by the time interval (in years) between the start of follow-up (initial diagnosis of IPMN) and the endpoint (date of surgical resection or latest medical follow-up visit prior to December 2016). In investigating the incidence of surgical resection, the above definitions for the beginning and endpoint of follow-up were used. Factors associated with surgical resection were analyzed retrospectively.

Statistical analysis

Categorical data are presented as numbers followed by percentages. Continuous data are presented as the mean± standard deviation (SD) or median (range). Normally distributed variables were compared between groups of patients who underwent and did not undergo surgical resection, such as pancreatectomy, using Student's t test, while non-normally distributed variables were compared using the Mann-Whitney U test. Frequency data were compared using a chi-squared test or Fisher's exact test, as appropriate. Cumulative incidence of surgical resection was calculated using the Kaplan-Meier method. Differences among patients who underwent and did not undergo surgical resection were assessed using the log-rank test. The time frame for surgical resection was defined as beginning at initial diagnosis of IPMN. The Cox proportional hazard model was used for multivariate analyses of factors associated with surgical resection. We determined cutoff values for factors associated with surgical resection using receiver operating characteristic analyses. Statistical analyses were performed using SPSS Statistics 21.0 (IBM SPSS., USA). A p value below 0.05 was considered to indicate statistical significance. Tests were 2-tailed.

Results

Baseline characteristics of enrolled patients

The mean age of the study subjects (85 male and 85 female) was 66 ± 11 years. IPMN were initially detected by US in 110 patients (65%), CT in 40 (24%), MRCP in 11 (6%), and by other methods in 6 (4%), including unknown methods in 3. Cyst numbers by site included 102 in the head, 124 in the body, and 64 in the tail. A single cyst was observed at onset in 43 patients, while multiple cysts were present initially in 127. Mean cyst size was 15.3 ± 8.9 mm in the head, 11.7 ± 6.9 mm in the body, and 9.8 ± 6.5 mm in the tail. Unilocular cysts numbered 93, while 77 cysts were multilocular. The mean MPD diameter was 2.3 ± 1.2 mm (**Table 1**).

Ability of US to detect IPMN relative to MRCP

For all cyst diameters, detection by US relative to MRCP was 60.8% (62/102) for the pancreatic head, 79.8% (99/124) for the body, and 32.8% (21/64) for the tail. Detection by US in the tail was significantly poorer than in the body ($p < 0.005$). US detection of cysts with diameters < 5 mm ($n = 25$) relative to MRCP was 100% (6/6) in the body and 23.1% (3/13) in the tail, again significantly poorer in the tail than in the body ($p < 0.01$). For cysts < 10 mm ($n = 111$), detection by US relative to MRCP was 75.4% (43/57) in the body and 17.2% (5/29) in the tail, representing a significant difference between sites ($p < 0.001$; **Fig. 1**).

Incidence of surgical resection in patients with IPMN

Among the 170 follow-up patients, 12 (7.1%) underwent surgical resection at some point. Their histopathologic tumor diagnoses were typical pancreatic cancer (2 patients), intraductal papillary mucinous carcinoma (IPMC) (3), and intraductal papillary mucinous adenoma (IPMA) (7). Indications for surgical resection were mural nodules (8 patients), cyst enlargement (2), presence of masses (2), and MPD stenosis (2; overlap exists). For the 12 follow-up patients who underwent resection, the mean observation period was 34 ± 29 months, mean cyst size at initial diagnosis was 24.4 ±

Table 1. Characteristics of Patients in Study

Characteristics	Patients
Age (years)	66 ± 10.7
Gender (female/male)	85/85
Mean observation period (months)	30 ± 19
Diagnostic modality	US 110 (65%)/CT 40 (24%)/MRCP 11 (6%)/Others 6 (4%)
Sites and numbers of cysts (head/body/tail)	102/124/64
Mean cyst size (mm; head/body/tail)	15.3 ± 8.9/11.7 ± 6.9/ 9.8 ± 6.5
Unilocular/multilocular	93/77
Single/multiple cyst(s) at onset	43/127
Mean diameter of MPD (mm)	2.3 ± 1.2

US: ultrasonography, CT: computed tomography, MRCP: magnetic resonance cholangiopancreatography, MPD: main pancreatic duct. Data are presented as mean ± SD for continuous variables and n (%) for categorical variables.

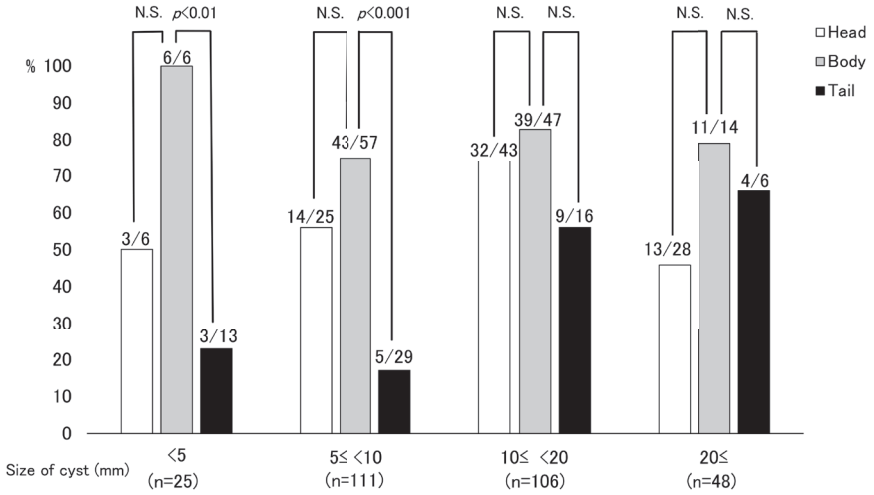

Fig.1. Depiction Ability of US for IPMNs Examined by Site and Size

Relative to Diagnosis of IPMN by MRCP, depiction ability of US for smaller IPMN (less than 5 mm) located in the pancreatic tail was significantly lower than for those located in the body (p<0.01). The depiction ability of US for slightly larger IPMN (more than 5 mm and less than 10 mm) in the tail was also significantly lower than in the body (p<0.001).

Table 2. Clinical and Imaging Findings During Follow-up : Surgical vs. Non-surgical Cases

Characteristics	Surgery (n=12)	No surgery (n=158)	p value
Age (years)	70.0 ± 7.88	66.0 ± 10.8	0.143
Gender (female/male)	8 (67%)/4 (33%)	78 (49%)/80 (51%)	0.248
Follow-up duration (months)	30 ± 19	40 ± 29	0.244
Unilocular/multilocular	7 (58%)/5 (42%)	85 (54%)/73 (46%)	0.761
Single/multiple cysts at onset	1 (8%)/11 (92%)	43 (27%)/115 (73%)	0.145
Sites and numbers of cysts (head and body/tail)	12 (100%)/0 (0%)	150 (95%)/8 (5%)	0.423
Cyst growth rate (mm/year)	0.69 ± 1.09	0.66 ± 1.41	0.944
Rate of increase in MPD diameter (mm/year)	0.41 ± 0.66	0.08 ± 0.31	<0.001
Mural nodules (present/absent)	4 (33%)/8 (67%)	2 (1.3%)/156 (98.7%)	<0.001
Masses (present/absent)	3 (25%)/9 (75%)	0 (0%)/158 (100%)	<0.001

"Surgery" refers to resections involving the pancreas at any time point in the course. MPD: main pancreatic duct. Data are presented as mean ± SD for continuous variables and n (%) for categorical variables.

14.5 mm, preoperative mean cyst size was 30.8 ± 20.3 mm, mean MPD diameter at initial diagnosis was 2.8 ± 1.0 mm, preoperative mean MPD diameter was 3.6 ± 1.9 mm, and preoperative mean size of nodules was 13.8 ± 12.3 mm.

Comparing US and MRCP with regard to the mural nodules found in 8 patients, they were detected by US in 3 patients (37.5%) and MRCP in 6 (75.0%).

Factors associated with surgical resection for IPMN

Among the 170 follow-up patients, 12 were surgery cases. Their characteristics were compared with those of the 158 non-surgery cases (**Table 2**). Significant dif-

ferences were observed between the two groups for rate of change in MPD diameter, presence of nodules, and presence of masses. Surgical resection was more likely in patients with an annual rate of increase in MPD diameter of ≥ 0.2 mm (**Fig.2**). Performing multivariate analysis by Cox proportional hazards regression with factors including age, gender, single vs. multiple cysts at onset, unilocular vs. multilocular cysts, cyst site, cyst growth rate, and rate of change in MPD diameter confirmed increase in MPD diameter by ≥ 0.2 mm/year and age ≥ 70 years to be factors significantly and independently associated with surgical resection in patients with IPMN (**Table 3**).

Discussion

MRCP, endoscopic US, abdominal CT, and abdominal US have been used for the diagnosis and follow-up of IPMN[2]. A previous study comparing US and CT for diagnosis found that US had significantly greater sensitivity than CT (96% vs. 33%)[3]. In another study, IPMN detection rates were approximately 20% for MRCP[4] and 3% for CT[5], demonstrating greater diagnostic ability for MRCP. However, the effectiveness of US vs. MRCP in patients with IPMN has remained an issue. The present study comparing the diagnostic capability of US and MRCP for IPMN demonstrated that US detection of IPMNs with diameters <10 mm in the pancreatic tail was significantly poorer than in the pancreatic body.

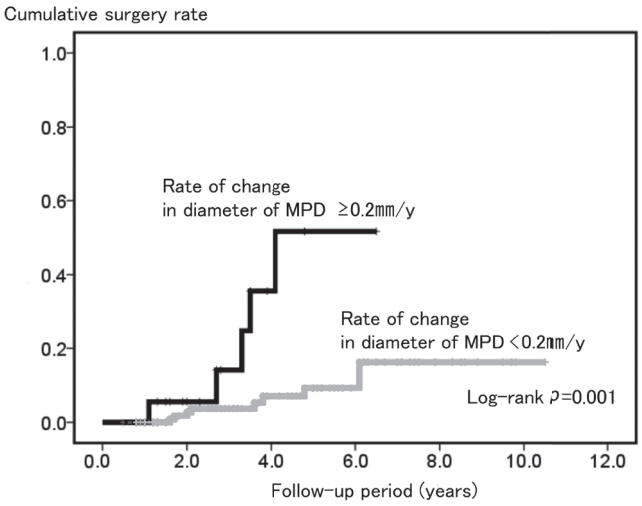

Fig.2. Cumulative Incidence Rates of Surgical Resection According to Rate of Change in the Diameter of MPD
The Maximum Diameter of The Main Pancreatic Duct (MPD) was Measured in Each Patient Using MRCP. The cumulative incidence of surgical resection in patients with higher rates of MPD diameter enlargement (≥ 0.2 mm/year) was significantly higher than that in patients with slower MPD diameter change (< 0.2 mm/year), based on Kaplan-Meier analysis and the log-rank test ($p < 0.001$).

Histopathologic diagnoses of branch-duct IPMNs include hyperplasia, IPMA, and IPMC, with a mean reported incidence for the carcinomas of 31.1% (14.4% to 47.9%)[6–12]. This risk of cancer underscores the importance of identifying factors predicting the need for resection of IPMN. The present study identified an increase in MPD diameter of ≥ 0.2 mm/year and an age of ≥ 70 years as significant independent factors associated with surgical resection in patients with IPMN. Prospective investigations in larger cohorts should provide more definitive evidence.

MRCP is the imaging modality best suited to diagnosis of IPMN. Specifically, MRCP has been advocated as the first choice for detailed examination of IPMN as it can delineate structures such as septa resulting in multiloculation, mural nodules, and communication with the MPD[13]. Among 16 of our surgical cases where mural nodules were observed within cysts, nodules were delineated by MRCP in 10 (62.5%), illustrating the superiority of MRCP.

As US is noninvasive and convenient, it is often used as the initial modality for screening. However, detection ability can be affected by body habitus and presence of gas in the alimentary canal, as well as the skill of the sonographer[14,15]. In particular, cysts in the pancreatic tail are not clearly delineated by US in many cases. This was demonstrated in the present study using MRCP as the standard by the relatively low US detection rate for IPMN in the tail (head: 60.8%, tail: 32.8%). As for CT, it involves radiation exposure and contrast resolution is poorer than with MRCP.

However, MRCP cannot be used for routine assessment in all cases. Disadvantages of MRCP include long examination time and need for considerable patient cooperation, such as having to hold the breath and remain still. In addition, MRCP may be contraindicated in some patients, for instance those with cardiac pacemakers[16].

Performing abdominal US as the first examination can provide valuable information, despite its shortcomings. One study found it highly useful for detecting pancreatic cysts with diameters ≥ 5 mm (sensitivity: 96%; specificity: 94%; diagnostic accuracy: 95%)[2].

Table 3. Factors Associated with Surgery by Cox Proportional Hazard Analysis

Characteristics	Category	Hazard ratio	95% CI	*p* value
Rate of increase in MPD diameter (mm/year)	< 0.2 ≥ 0.2	7.32	2.30–23.36	0.001
Age (years)	< 70 ≥ 70	3.26	1.08–9.85	0.036

CI: confidence interval, MPD: main pancreatic duct.

When cystic lesions detected by US are suspected to be IPMN, depending on cyst size and location, follow-up examination by MRCP can be performed if not contraindicated. (Respiratory triggering of MRCP image acquisition might reduce need for holding the breath in some patients.)

Our retrospective study design imposed some limitations. Not all patients diagnosed with IPMN had undergone both US and MRCP. In addition, examination intervals varied among subjects. Prospective studies involving large numbers of patients with IPMN are needed.

Conclusion

In the pancreatic tail, US was less able to depict small cysts than MRCP. As multiple lesions are common with IPMN, US detection of cysts in the pancreatic head or body should be followed by MRCP when possible, particularly for detection of any cysts in the tail that might otherwise be missed. Patients with relatively rapid increases in MPD diameter and older individuals must be monitored closely, as they may require surgical resection.

Financial Disclosure

The authors declare that they have nothing to disclose regarding funding or conflicts of interest with respect to this manuscript.

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(Received May 17, 2019 ; Accepted July 5, 2019)