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Original Article

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Transabdominal Ultrasound Detection of Pancreatic Cystic Lesions with Reference to Previous Magnetic Resonance Imaging

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Abstract

Objective: Pancreatic cystic lesions (PCLs) should be carefully followed up because they are transabdominal ultrasound (TAUS) findings indicating a high-risk of pancreatic cancer. The aim of this study was to investigate the usefulness of follow-up TAUS for PCL surveillance, with reference to previous magnetic resonance imaging (MRI).

Methods: The hospital database for 781 subjects who underwent a health check-up including MRI was searched. The PCL detection rate and the size of their maximum dimension in follow-up TAUS after MRI were examined. Subjects with and without detected PCLs in follow-up TAUS were statistically compared for clinical characteristics.

Results: The detection rate for PCLs that were invisible in the initial TAUS was 21.9% in follow-up TAUS after MRI and 68.7% of these PCLs were under-measured, with a size difference of −1.8 ± 3.7 mm. Multivariate logistic regression analysis showed that visualization of PCLs by follow-up TAUS was significantly associated with PCL size and the presence of fatty liver (OR, 95% CI, *p*: 1.477, 1.252–1.741, 0.000; 0.252, 0.088–0.725, 0.011). On the other hand, with a detection rate of 97.5% for the visible PCLs in the initial TAUS, the reproducibility of follow-up TAUS was very high, although 51.3% of these PCLs were under-measured, with a size difference of −1.3 ± 2.3 mm.

Conclusions: The PCL detection rate for follow-up TAUS after MRI improved in approximately 20% of subjects with invisible PCLs in the initial TAUS, and high reproducibility was demonstrated for TAUS. It should be noted that PCL size could be under-measured in TAUS, after MRI.

Keywords pancreatic cystic lesion, follow-up transabdominal ultrasonography, magnetic resonance imaging

There are several risk factors for pancreatic cancer, 2 of them family history and diabetes mellitus. Others are chronic pancreatitis and pancreatic cystic lesions (PCLs), including intraductal papillary mucinous neoplasia (IPMN), that should be carefully followed up as premalignant diseases of pancreatic cancer, according to the guidelines for pancreatic cancer issued by the Japan pancreas society in 2013[1]. Although PCLs are often detected incidentally, especially through the widespread use of magnetic resonance imaging (MRI), cysts with invasive carcinoma are rarely found in asymptomatic individuals. Transabdominal ultrasonography (TAUS) is useful in initial screenings as well as in health check-ups, and is also a first choice for pancreatic diseases due to its great convenience, non-invasiveness, and cost effectiveness[2,3]. However, the entire pancreas is difficult to visualize clearly using TAUS because of its deep retroperitoneal location as well disruption of ultrasound transmission due to body habitus and interposed bowel gas[4]. On the other hand, MRI with T2-weighted images and magnetic resonance cholangiopancreatography (MRCP) are considered to be the best imaging modality for detecting PCLs due to their superior contrast resolution and ability to highlight fluid-containing structures[5]. According to the 2015 American Gastroenterological Association institute guideline, MRI is an appropriate surveillance imaging tool for cysts less than 3 cm without a dilated pancreatic duct or a solid component[6]. However, this modality is lengthy, there are people who are contraindicated and it increases medical

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costs when used for follow-up.

Recently, 2 studies regarding the detection rate of TAUS for known PCLs using MR and other correlative images, have been published[7,8]. They concluded that TAUS could be a useful surveillance imaging tool for PCLs because the majority of PCLs were visualized and accurately measured in follow-up TAUS using the correlative images. Therefore, we investigated whether the PCL detection rate was improved by follow-up TAUS with reference to previous MRI findings in our cohort[9]. Its members had been reported to have PCLs based on an optional MRI examination in a health check-up.

Materials and Methods

Subjects

The Institutional Review Board of Keio University Hospital approved this retrospective study and the requirement for informed consent was waived (IRB No. 20160398). We used the same hospital database as the one that had been used for analysis in our previous study[9]. We searched the medical records, including demographics, medical history, the presence of metabolic syndrome, body mass index (BMI), waist circumference (WC), subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT), and blood tests as well as TAUS and MRI reports for consecutive subjects who underwent a health check-up at our facility for the first time between August 2012 and July 2016.

Image acquisition for US, MRI and CT, and image analysis

All the subjects had been fasting overnight when they underwent the screening TAUS examination in the supine or right and left lateral position, not the sitting position, using a Logiq S8 system (GE Healthcare, USA) with 3–6 MHz wide band convex probe. The initial TAUS was performed by an experienced sonographer in the digestive area, who was accredited by the Japan Society of Ultrasonics in Medicine, before the initial MRI examination performed at a maximum of 3 months later, and used color Doppler ultrasonography (US) and a linear probe, if required. In our facility, US was not performed by a method that involved drinking water. Examination time was approximately 10 minutes and the size of the lesion found in TAUS was measured using two dimensions in a magnified image. The TAUS results were available only from the subjects' formal records. They had been confirmed by a radiologist and included the size and the location of the detected pancreatic cyst with the maximum dimension among all detected PCLs. Fatty pancreas was diagnosed when the pancreas was observed to be hyperechoic in comparison with echogenicity in the left lobe of the liver. The PCL detection rate in follow-up TAUS with reference to the initial MRI report was calculated. We also compared the result of follow-up TAUS with that for follow-up MRI carried out within a maximum of 3 months after follow-up TAUS. Thus, this study includes the data from one follow-up TAUS and the subsequent follow-up MRI.

The upper abdominal MRI examination was performed on a 1.5 Tesla clinical scanner (Signa HD xt; GE Healthcare, USA) according to the standard department protocol including the following sequences: (1) 3 plane localizer, (2) axial and coronal single-shot fast/turbo spin-echo (SSFSE), (3) Fat-suppressed T2-weighted fast spin echo (FSE), (4) 3D MRCP in rotating coronal oblique orientations. Chemical shift imaging with dual echo T1-weighted gradient-recalled echo in-phase and out-of-phase sequences were also obtained. No intravenous contrast was administered in this cohort. Image analysis was performed on a PACS system (Centricity; GE Healthcare, USA) by 2 independent readers and reviewed in consensus. The MRI results were used as reference standard for the size and location of PCLs in the pancreas.

We reevaluated the image of the pancreas in non-enhanced chest CT performed routinely to screen for chest lesions in order to determine the presence of pancreatic atrophy using a protocol[10], in the absence of information from the TAUS or MRI reports. Pancreatic atrophy was defined as a pancreatic body width of less than 10 mm. Also, routine fat CT was performed at the umbilicus level to measure WC, SAT and VAT, with calculations made using AZE Virtual Place software (AZE Inc., Tokyo, Japan), as previously reported[11].

Statistical analysis

Statistical analyses were performed using SPSS software version 24 (SPSS, Inc., USA). Statistical differences between two groups were determined using the t-test or Mann-Whitney U test for continuous data, and the chi-square test for categorical data, when MRI was considered as the reference standard. Continuous data were presented as the means ± standard deviation. Parameters with a p value of less than 0.05 in the univariate analysis were candidates for the multivariate logistic regression analysis applied to determine factors, which were associated with PCL visualization in TAUS. A p value < 0.05 was considered statistically significant.

Results

Study population and PCL detection rate in follow-up TAUS

The flow chart of the present study is shown in **Fig. 1**. Of the total of 781 subjects enrolled in this study, PCLs were detected in 139 subjects in the initial MRI, including 98 subjects diagnosed as having Intraductal Papillary Mucinous Neoplasm (IPMN), as previously reported[9]. Among them, 56 and 83 subjects, respec-

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tively, were diagnosed with PCL and without PCL in the initial TAUS, before the initial MRI[12]. Sixteen and 10 subjects, respectively, were eliminated from these 2 groups, as they had not undergone a follow-up examination within a maximum period of 3 months of each other. Therefore, 40 and 73 subjects in these 2 groups, who had undergone both TAUS and MRI for follow-up, were included in this study. All of them had no history of chronic pancreatitis or other pancreatic diseases. Thirty-nine subjects with visible PCLs and 16 subjects with invisible PCLs in the initial TAUS were diagnosed with PCLs in the follow-up TAUS. **Fig. 2** shows images for a 60-year-old male with IPMN in the pancreatic body. The MRI and MRCP images reveal a cystic mass connected to the main pancreatic duct (A and B). Although the cystic lesion could not be detected in the axial view (C1), or sagittal view (C2) of the initial TAUS, it was successfully detected in follow-up TAUS, with reference to the initial MRI report, in the axial view (D1) and sagittal view (D2). The overall PCL detection rate in the follow-up TAUS was 48.7% (55/113) in contrast to that of 35.4% (40/113) in the initial TAUS. The detection rates by region (head, body and tail) of the pancreas were 64.4 (= 29/29+16)%, 34.1 (= 14/14+27)%, and 44.4 (= 12/12+15)%, respectively, as shown at the bottom of **Table 1**. Only one small cyst (5 mm) found in the initial TAUS could not be detected in the follow-up TAUS, although it was also observed in the follow-up MRI. Thus, the reproducibility of the follow-up TAUS for initially visible PCLs was very high (39/40 = 97.5%), whereas the detection rate in follow-up TAUS after the initial MRI for invisible PCLs in the initial TAUS was just 21.9% (16/73) (**Fig. 1**).

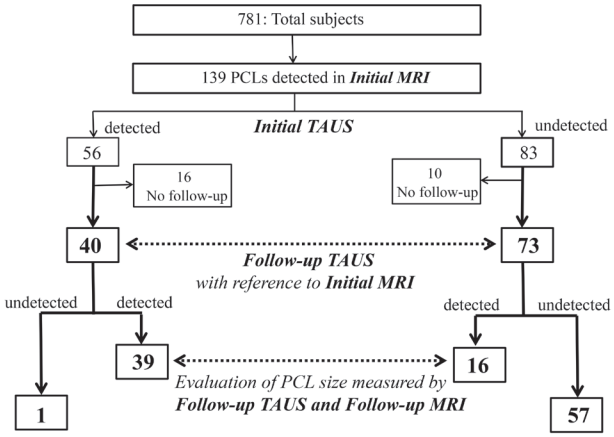

Fig1. Flow Chart and Numbers of PCLs Detected by TAUS in Present Study

PCLs: pancreatic cystic lesions, MRI: magnetic resonance imaging, TAUS: transabdominal ultrasonography.

Comparison of clinical characteristics between subjects with detected and undetected PCLs in follow-up TAUS after initial MRI

As shown in **Table 1** and **Table 2**, we compared 55 subjects with PCLs detected by follow-up TAUS and 58 subjects in whom PCLs were not detected. The former group was significantly older (68.2 vs 64.8 years, p = 0.047) and tended to have smaller WC, SAT, and VAT than the latter group, but differences were not significant. The former group had more PCLs in the head of the pancreas (54% vs 28%, p = 0.017), and fatty liver

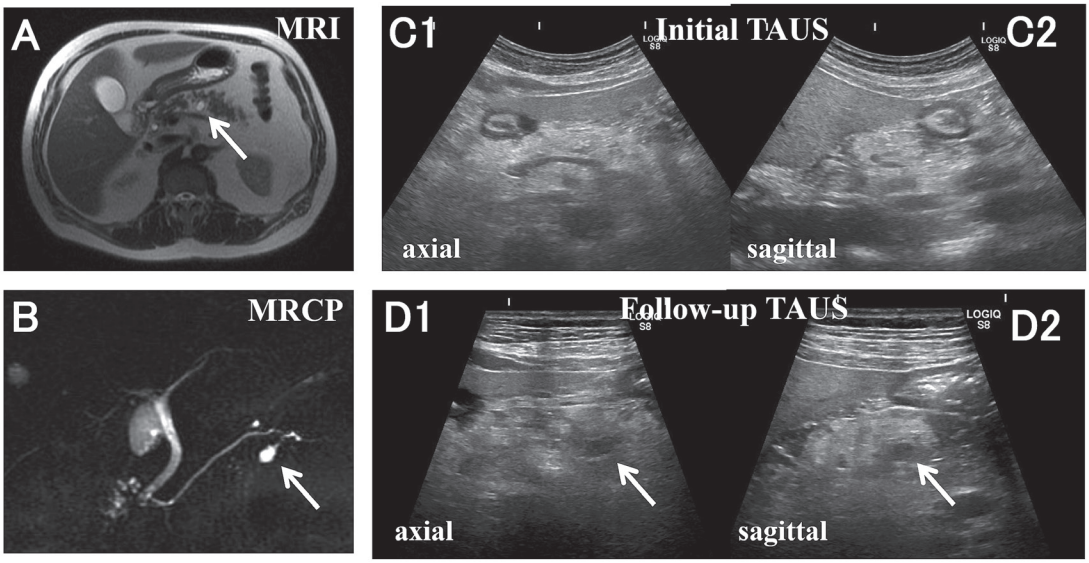

Fig.2. IPMN Detected in Pancreatic Body of 60-year-old Male

(A) Transverse T2-weighted image in MRI demonstrated a cystic mass in the body of the pancreas. (B) MRCP revealed that this cystic lesion was connected to the main duct of the pancreas. (C1 and C2) The cystic lesion could not be detected in an axial view (C1), or sagittal view (C2) in the initial TAUS. (D1 and D2) With reference to the initial MRI report, the lesion could be detected by follow-up TAUS in an axial view (D1) and a sagittal view (D2).
MRI: magnetic resonance imaging, MRCP: magnetic resonance cholangiopancrea-tography, TAUS: transabdominal ultrasonography, IPMN: Intraductal Papillary Mucinous Neoplasm.

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Table 1. Comparison of Clinical Characteristics between Subjects with and without PCLs Detected by Follow-up TAUS after Initial MRI

Characteristics	Subjects with PCLs detected by follow-up TAUS (n = 55)	Subjects with no PCLs detected by follow-up TAUS (n = 58)	Univariate Analysis p	Multivariate Analysis p OR (95%CI)
Age, years	68.2 ± 7.6	64.8 ± 10.1	0.047	0.053
Male, *n* (%)	34 (61.8)	44 (75.9)	0.107	
Metabolic synd., *n* (%)	16 (29.1)	15 (25.9)	0.701	
Fatty liver, *n* (%)	16 (29.1)	29 (50.0)	0.023	0.011 0.252 (0.088–0.725)
Fatty pancreas, *n* (%)	13 (23.6)	14 (24.1)	0.950	
Atrophic pancreas, *n* (%)	4 (7.3)	7 (12.1)	0.390	
Body mass index, kg/m^2	22.7 ± 2.9	23.5 ± 2.6	0.127	
WC, cm	81.3 ± 8.0	84.2 ± 8.3	0.055	
SAT, cm^2	144.4 ± 57.3	151.7 ± 55.3	0.496	
VAT, cm^2	101.5 ± 47.6	112.8 ± 45.0	0.198	
PCL size, mm	12.7 ± 6.7	6.2 ± 2.6	0.000	0.000 1.477 (1.252–1.741)
PCL location (Head, Body, Tail), *n* (%)	29, 14, 12 (55, 25, 22)	16, 27, 15 (28, 46, 26)	0.017	0.265

PCL: pancreatic cystic lesion, TAUS: transabdominal ultrasonography, WC: waist circumference, SAT: subcutaneous adipose tissue, VAT: visceral adipose tissue.

Table 2. Numbers (percentages) of Subjects with and without PCLs Detected by Follow-up TAUS after Initial MRI, According to PCL Size

Size (maximum dimension)	Number (%) of subjects with PCLs detected by follow up TAUS (n = 55)	Number (%) of subjects without PCLs detected by follow-up TAUS (n = 58)	p
< 10 mm	25 (45.5)	55 (94.8)	0.000
10 mm ≤	30 (54.5)	3 (5.2)	

PCL: pancreatic cystic lesion, TAUS: transabdominal ultrasonography.

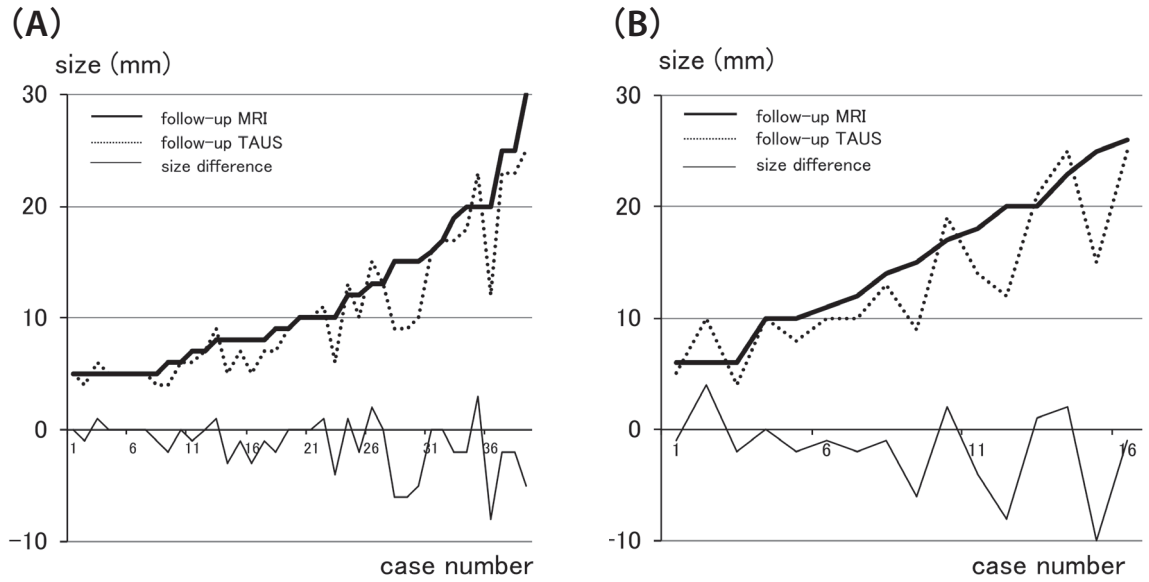

Fig.3. PCL Size Measured in Follow-up MRI and Follow-up TAUS, and Size Difference between the Two Modalities

(A) For 39 PCLs detected in the initial TAUS, the bold line, dotted line and thin line show the sizes measured in follow-up MRI and follow-up TAUS and size difference between the two modalities, respectively.

(B) For 16 PCLs not detected in the initial TAUS, the bold line, dotted line and thin line show the sizes measured in follow-up MRI and follow-up TAUS and size difference between the two modalities, respectively.

MRI: magnetic resonance imaging, PCL: pancreatic cystic lesion, TAUS: transabdominal ultrasonography.

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was less frequent than in the latter group (29.1% vs 50%, $p = 0.023$). Additionally, PCLs were not detected by follow-up TAUS if they were smaller (12.7 vs. 6.2 mm, $p = 0.000$; size <10 mm vs. 10 mm ≤ size, $p = 0.000$).

The results of multivariate logistic regression analysis are shown in the far right column of **Table 1**. Presence of fatty liver and PCL size were factors significantly associated with visualization of PCLs in follow-up TAUS (Odds Ratio (OR): 0.252, 95% Confidence Interval (CI): 0.088–0.725, $p = 0.011$; OR: 1.477, 95% CI: 1.252–1.741, $p = 0.000$).

Evaluation of PCL size measured in both TAUS and MRI for follow-up

We also examined the difference in PCL size measured in follow-up TAUS and follow-up MRI for 39 subjects with initially detected PCLs and 16 subjects without them, who underwent both examinations within 3 months of each other (**Fig. 3A**, **3B**). Twenty (51.3%) of the 39 PCLs were under-measured with a size difference of −1.3 ± 2.3 mm (−8 to + 3 mm). In addition, 11 (68.7%) of the 16 PCLs were under-measured with a size difference of −1.8 ± 3.7 mm (−10 to + 4 mm). However, there was no significant difference in PCL size difference between the two groups ($p = 0.524$).

Discussion

This study has 3 main findings. First, the overall PCL detection rate increased from 35.4% (40/113) to 48.7% (55/113) in the follow-up TAUS after MRI, with TAUS showing high reproducibility with respect to the initial TAUS. Our results suggest that undetected PCLs of 10 mm or more in size that were not detected in the initial TAUS could be detected in follow-up TAUS after MRI, and there is the possibility of this increasing when they are located in the pancreatic head. On the other hand, the previous MRI reports probably did not contribute to the detection of PCLs of less than 10 mm, because the detection rate for these PCLs in the initial TAUS was only 30%[12]. Although it seems that TAUS specialists were able to determine the presence of PCLs more confidently using MRI for reference, even when the TAUS image was obscured by adipose tissue and/or intestinal gas, the increase in detection rate in our cohort was much lower than that in the study of Jeon *et al.*[7], which found a significant improvement in detection, from 49.2 to 86.7%. This might be mainly because there was a larger percentage of smaller PCLs in our study than in theirs.

Second, there were no significant associations between PCL visualization in follow-up TAUS and obesity-related factors (BMI, WC, SAT and VAT). However, presence of fatty liver was significantly associated with invisibility of PCLs in follow-up TAUS, which is similar to the result obtained in our recent study[12] and shows that coexisting fatty liver may have lowered PCL detection rates in the initial TAUS.

Third, PCL size was under-measured in the follow-up TAUS for 68.7% of PCLs that were invisible in the initial TAUS. Sun *et al.*[8] conducted a prospective study which showed that under-measurement was slightly more common than over-measurement with TAUS (46 vs. 31%). They also found that the maximum diameter measured by TAUS was smaller by only 0.7 mm on average, compared to that measured by MRI. Also, Kang *et al.*[13] reported that cysts growing faster than 2 mm/year had 3- and 5-year cumulative risks of malignancy of 6.4% and 45.5%, whereas cysts growing less than 2 mm/year had corresponding risks of 1.8 and 1.85%, respectively, in their cohort, which included patients with side-branch IPMN and an initial size of less than 30 mm without main pancreatic duct (MPD) dilatation or mural nodules. In addition, the 2017 revisions of international consensus Fukuoka guidelines[14] recommend surveillance of PCLs depending on the size estimated by an imaging modality. Furthermore, the most recent American College of Gastroenterology (ACG) clinical guideline[15] states that patients with a rapid increase in cyst size of > 3 mm/year should undergo short-interval MRI.

The entire pancreas is indeed difficult to examine using TAUS and the procedure is operator-dependent. Obtaining objective data accurately and reproducibly for cyst dimensions is also difficult with TAUS in the clinical setting. In the present study, there is a high possibility that a considerable number of PCLs were obscured in TAUS and the size may have been under-measured due to overlying gas or adipose tissue. IPMNs are often pleomorphic or clustered, which might cause difficulty in accurate size measurement using an imaging modality. The largest single cyst in a cluster may be measured by TAUS, resulting in under-measurement of size, because it is considered unlikely that all of the individual cysts in a cluster will be fully visualized with TAUS. Thus, accurate evaluation of cyst size during surveillance with a particular imaging modality is important not only for reducing variability in size measurement between modalities but also with regard to risk stratification and clinical decision making.

The limitations of this study include its retrospective design, the fact that it was conducted at a single institution and its relatively small sample size. Also, the use of a linear probe or longer examination time in follow-up TAUS after MRI may have contributed to the higher PCL detection rate. Therefore more prospective research is needed to validate the utility of follow-up TAUS after MRI for detection of known PCLs.

Conclusions

The detection rate for PCLs in follow-up TAUS with

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reference to MRI improved in approximately 20% of subjects with invisible PCLs in the initial TAUS and the reproducibility of TAUS with respect to the initial TAUS was very high (97.5%). It should be noted that PCL size can be under-measured by TAUS with reference to MRI.

Conflict of Interest

All authors report that they have no disclosures relevant to this publication to make.

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