Metabolic Syndrome Accelerates the Age-Related Increase of Intraductal Papillary Mucinous Neoplasm of the Pancreas

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Metabolic syndrome accelerates the age-related increase of intraductal papillary mucinous neoplasm of the pancreas

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Abbreviations:

BMI: body mass index; CI: confidence interval; CT: computed tomography; DM: diabetes mellitus; EUS: endoscopic ultrasonography; HL: hyperlipidemia; HT: hypertension; IPMN: intraductal papillary mucinous neoplasm; MDCT: multi-detector row computed tomography; MRCP: magnetic resonance cholangiopancreatography; MRI: magnetic resonance imaging; MS: metabolic syndrome; OR: odds ratio; PanIN: pancreatic intraepithelial neoplasia, PDAC: pancreatic ductal carcinoma; US: ultrasonography

Author contributions

S.T. corrected and analyzed the data and S.T. and M.T. wrote the manuscript together with A.M. designed the study; T. F., J.I., H.S., A.S, T.K., R.N., Y.Y., T.T., S.A., K.Y., S.A.,

M.G., S.M., N.I., H.U., K.N., and S.K. collected, analyzed, and interpreted the data. K.F., T. A., A.W., and Y.K. supervised the study and revised the manuscript accordingly.

Declaration of competing interest

The authors have no conflicts of interest.

ABSTRACT

Objectives: Aging is associated with a high prevalence of pancreatic cysts and intraductal papillary mucinous neoplasms (IPMNs). Metabolic syndrome (MS) may increase the risk of neoplasms, including those that develop in the pancreas. However, the influence of factors associated with MS on the development of IPMN remains unclear.

Methods: A total of 9363 patients who underwent abdominal ultrasound examinations between April 2012 and May 2013 were included in this study. Multivariate logistic regression analysis was performed to identify factors associated with the presence of IPMN by age.

Results: Pancreatic cysts were detected in 198 of 9,363 patients, of whom 129 were found to have IPMNs. The presence of IPMN significantly correlated with age (10-year increments; OR 2.73, 95% CI 2.28–3.29; $p<0.001$). High body mass index (BMI), history of smoking, hyperlipidemia (HL), hypertension (HT), and MS were associated with a higher prevalence of IPMN with advancing age. In multivariate analysis, the presence of IPMN was more frequent in elderly patients with MS (OR, 3.14; 95% CI 3.14–6.72; $p=0.003$).

Conclusions: The present study suggests that the incidence of IPMN increases with age and is accelerated in the presence of MS.

Keywords:

health screening, intraductal papillary mucinous neoplasm, metabolic syndrome, magnetic resonance imaging

INTRODUCTION

Currently, pancreatic cysts, including intraductal papillary mucinous neoplasms (IPMNs), are routinely detected because of rapid advancements in multidetector-row computed tomography (MDCT) and high-resolution magnetic resonance imaging (MRI) [1-4]. Pancreatic cysts, particularly IPMNs, have recently been recognized as precursors of pancreatic ductal carcinoma (PDAC) [5, 6]. Some IPMNs progress to pancreatic carcinoma, whereas other IPMNs occur concomitantly with conventional PDAC, which arises from the pancreatic intraepithelial neoplasia (PanIN) pathway. A recent report indicated that the 3- and 5-year incidence rates of IPMN-concomitant PDAC were 4.0% and 8.8%, respectively [7]. Another study reported that the 5-year incidence rate of pancreatic malignancy was 3.3%, reaching 15.0% 15 years after IPMN diagnosis [8]. Therefore, understanding the etiology and risk factors of IPMNs is important for detecting or preventing pancreatic malignancies.

Three previous studies examined the risk factors for pancreatic cysts, and two studies examined the risk factors for IPMNs [2, 9-12]. In four of the five studies, aging was associated with a higher prevalence of pancreatic cysts or IPMNs, whereas both old age and female sex were associated with a higher prevalence of IPMNs in the fifth study. These results suggest that old age may be a definitive risk factor for pancreatic cysts or IPMNs; however, the influence of patient comorbidities on the prevalence of IPMN remains unknown.

Obesity and metabolic syndrome (MS) may be associated with an increased risk of neoplasms, such as pancreatic and colorectal cancers [13, 14]. However, the relationship between obesity and IPMN, a precancerous lesion of PDAC, has not been clarified. Similarly, risk factors for IPMNs have not yet been fully analyzed. Therefore, this study

aimed to identify the risk factors for the prevalence of and age-related increase in IPMN.

METHODS

Patients

From October 2012 to October 2013, patients who underwent abdominal ultrasonography (US) during health screenings at the Yodogawa Christian Hospital participated in the study. Patients in whom the pancreas could not be adequately observed on abdominal ultrasonography were excluded from the study.

Definition of US and MRI findings

Positive findings of the pancreas on US were classified into three categories: pancreatic cysts, pancreatic duct dilatation, and hypoechoic lesions of the pancreas. Pancreatic cysts were defined as cystic lesions in the pancreas, pancreatic ductal dilatations were defined as dilatations of 2 mm or larger in the main pancreatic duct, and hypoechoic lesions were defined as recognizable hypoechoic nodules as compared with a normal pancreas.

'Presence of pancreatic cyst' was defined as a subject for whom a pancreatic cyst could be detected by both US and MRI examination, and 'Absence of pancreatic cyst' was defined as a subject for whom a pancreatic cyst was not present despite adequate observation of the pancreas by US. The diagnostic criteria for IPMN were pancreatic cysts measuring 5 mm or larger, with the presence of communication with the main pancreatic duct or the presence of a multilocular form. The diagnostic criteria for IPMN were in accordance with the revised international consensus Fukuoka guidelines for the management of pancreatic IPMN [15]. Trained technicians performed all US examinations. The findings were reevaluated by a gastroenterologist (T.F.), who was blinded to the clinical features of the individuals. Magnetic resonance cholangiopancreatography (MRCP) findings were first reviewed by a radiologist, and the

MRI images of all cases were re-reviewed by a blinded second reviewer (S.T.).

Outcomes and evaluation items

This study aimed to identify the risk factors for the prevalence and age-related increase in IPMN. The health screening questionnaire collected demographic and health information, including age, sex, body mass index (BMI), smoking and drinking history, and personal history of chronic diseases, such as hypertension (HT), hyperlipidemia (HL), diabetes, and MS. Based on the Japanese Committee for the Diagnostic Criteria of MS [16], MS was defined as the presence of central obesity (waist circumference ≥85 cm in men and ≥90 cm in women) and two or more of the following risk factors: lipid abnormalities (triglyceride (TG) ≥150 mg/dL and/or HDL-C <40 mg/dL or use of medication for dyslipidemia), high blood pressure (systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥85 mmHg or use of medication for hypertension), and hyperglycemia (fasting plasma glucose ≥110 mg/dL or use of medication for diabetes mellitus). The following information about pancreatic cysts was also collected: cyst size (in cases of multiple cysts, the diameter of the largest cyst), cyst location (head, body-tail, or diffuse), presence of mural nodules, diameter of the main pancreatic duct, and thickened enhancing wall of the cyst.

The study protocol was reviewed and approved by the Ethics Committee of Yodogawa Christian Hospital (No. 2020-12). This study was conducted in accordance with the principles of the Declaration of Helsinki (UMIN-CTR ID:000040907). All authors had access to the study data, and reviewed and approved the final manuscript.

Statistical analysis

All statistical analyses were conducted using SPSS version 27 (IBM, Armonk, NY, USA), and all p-values were two-sided. Student’s t-test was used to assess relationships

involving continuous variables, and a chi-square test (or Fisher's exact test, where appropriate) was used to evaluate relationships involving nominal variables. Multivariate logistic regression analysis was used to model predictors of pancreatic cysts or IPMNs by age. In all analyses, $p<0.05$ was considered to indicate statistical significance.

RESULTS

Frequency of pancreatic cyst and IPMN in study participants

From October 2012 to October 2013, 15,859 individuals underwent abdominal ultrasonography (US) during health screenings at the Yodogawa Christian Hospital. Individuals whose pancreas could not be completely visualized were excluded (n=6,408). Among the individuals whose pancreas could be completely visualized using abdominal US (n=9,451), 233 pancreatic cysts, 31 main pancreatic duct dilatations, and 22 pancreatic hypoechoic lesions were identified. Of these individuals, those who did not undergo MRCP (n=44) and those whose pancreatic cysts were not detected by MRCP (n=44) were excluded. Ultimately, 9,363 individuals were included in the study. We classified the study participants as "pancreatic cyst present (n=198)" or "pancreatic cyst absent (n=9,165)", in which the pancreatic cyst was detected by abdominal US and confirmed by MRCP. The 198 patients with pancreatic cysts were further classified into IPMN and non-IPMN groups (**Figure 1**). The "pancreatic cyst present" cases were further divided into two groups: IPMN suspected cases (IPMN cases: n=129) and non-suspected cases (non-IPMN cases: n=69). The prevalence rates of pancreatic cysts and IPMN were found to be 1.4% (129/9363) and 2.1% (198/9363), respectively. Other pancreatic cystic neoplasms such as serous and mucinous cystic neoplasms were not identified in this cohort.

Further evaluation of individuals without pancreatic cysts

Among individuals without pancreatic cysts according to abdominal US findings (n =9,165), 378 individuals required further evaluation due to abnormal US findings in organs other than the pancreas (e.g., gall bladder polyp). Among these 378 individuals, 235 underwent MRI, and 68 underwent computed tomography (CT) (**Supplemental Table 1**). Abnormal findings in organs other than the pancreas were classified as follows: 139 liver cases, 14 bile duct cases, 80 gallbladder cases, 42 urinary system cases, six adrenal gland cases, two spleen cases, and 20 cases involving other organs. Pancreatic cysts were detected using additional MRCP or CT in 5.2% (16/303) of patients who underwent further evaluation, while 94.8% (287/303) did not have pancreatic cysts.

Factors associated with a pancreatic cyst and IPMNs

To assess the risk factors for pancreatic cysts or IPMN, we performed a multivariate binary logistic regression analysis, adjusting for potential confounders. The binary categorical variable, the absence or presence of a pancreatic cyst or IPMNs, was used as an outcome variable. In the analysis of pancreatic cysts, the odds ratio was adjusted for age and the presence of HT, HL, and diabetes, which were significantly associated with the presence of pancreatic cysts in the univariate analysis (**Table 1**). In the analysis of IPMN, the odds ratio was adjusted for age (continuous variable), BMI, and the presence of HT, HL, and diabetes, which were significantly associated with the presence of IPMN in the univariate analysis (**Supplemental Table 2**). Univariate analysis showed that the presence of pancreatic cysts was significantly correlated with old age ($p<0.001$), HT ($p<0.0001$), HL ($p<0.001$), diabetes ($p<0.001$), and MS ($p=0.001$). The presence of IPMNs also significantly correlated with old age ($p<0.001$), HT ($p<0.001$), HL ($p<0.001$), diabetes ($p<0.001$ and MS ($p<0.001$).

Multivariate logistic regression analysis of factors associated with pancreatic cysts and

IPMN (**Tables 2 and 3**) revealed that the presence of pancreatic cysts was significantly correlated with age (10-year increments; multivariable OR 2.58, 95% CI, 2.23–2.99; p<0.001). The presence of IPMN was also significantly correlated with age (10-year increments; OR 2.73, 95% CI 2.28–3.29; p<0.001). In addition, a high BMI was marginally, but significantly, associated with the presence of IPMN (BMI≥25; OR 1.53, 95% CI 0.95–2.41; p=0.080) but not with the presence of non-IPMN. In the comparison of the morphological characteristics of IPMN and non-IPMN (**Table 4**), a larger cyst size, multilocular form, and communication with the main pancreatic duct were more frequently observed in IPMN (p<0.001, p<0.0001, and p<0.001, respectively).

The influence of metabolic syndrome and its associated factors on the age-related increase of IPMN

The presence of pancreatic cysts and IPMNs among the different age groups was analyzed and is shown in **Figure 2.** The prevalence of pancreatic cysts increased with age (p<0.001). The highest prevalence of IPMNs was observed in individuals aged over 70 years (6.6%). However, subjects aged 20–29 years had a prevalence of 0%, whereas those aged 30–39 years had a prevalence of 0.2%.

The influence of underlying comorbidities and other patient characteristics on the frequency of IPMN in different age groups was also examined. As the age of patients increased, the number of IPMNs increased. To analyze the influence of metabolic syndrome and its associated factors on age-related increase in IPMN, the frequency of IPMN in each factor subgroup was compared among different age groups. The incidence of IPMN was higher in patients with high BMI, history of smoking, dyslipidemia (DL), hypertension (HT), and MS (**Figure 3**). Next, we focused on patients in their 60s (n=1,543). The predictive factors of a higher frequency of IPMN detection included high

BMI (OR 2.07; 95% CI 1.04–4.13), past or current smoking (OR 1.89; 95% CI 1.07–3.35), the presence of HL (OR 1.88; 95% CI 1.04–3.38), the presence of HT (OR 2.32; 95% CI 1.30–4.16), and the presence of MS (OR 4.08; 95% CI 2.02–8.23). Furthermore, in the multivariate analysis, the presence of metabolic syndrome was independently associated with a high incidence of IPMN (OR, 3.14; 95% CI 1.47–6.72; p=0.003; **Table 5**).

Incidence of pancreatic neoplasm (PDAC or P-NEN)

During the initial screening using abdominal US, 22 low-echoic lesions of the pancreas were identified. PDAC and pancreatic neuroendocrine neoplasm (P-NEN) were not identified in these lesions. In this cohort, 129 individuals with IPMN were followed up (median follow-up period: 36 months). One PDAC case and one P-NEN case were identified 3 and 2 years after the first screening, respectively. In the PDAC case, the IPMN was distributed throughout the pancreas, with no mural nodules or dilation of the main pancreatic duct.

DISCUSSION

In this large-scale retrospective study, we analyzed 9,363 subjects who underwent abdominal US for health screening. The present study showed that the prevalence of IPMN increased with age and that metabolic syndrome was associated with IPMN prevalence, especially in subjects in their 60s. Similar to previous reports, advanced age was significantly associated with IPMN prevalence in the multivariate logistic regression model. Several studies have revealed that obesity and MS may increase the risk of developing several types of neoplasms including PDAC. Recently, IPMNs have been recognized as PDAC precursors. However, few studies have investigated the influence of MS and its associated factors on IPMN prevalence. To the best of our knowledge, this is

the first study to investigate these associations.

Several previous studies have reported the risk factors for pancreatic cysts or IPMNs. Three studies examined the risk factors for pancreatic cysts, and two studies examined the risk factors for IPMNs. Laffan *et al.* reviewed 2,832 contrast-enhanced MDCT scans of the abdomen in outpatients and reported a strong correlation between pancreatic cysts and age [2]. Zanini *et al.* examined 762 contrast-enhanced CT scans conducted over one year at a state hospital and found that the prevalence of cysts was correlated with increasing age, with a prevalence of up to 13.4% (95% CI 6.6–20) in individuals aged 80–89 years ($p<0.001$) [12]. Kromrey *et al.* recruited 1077 participants (521 men, mean age 55.8±12.8 years) from the population-based Study of Health in Pomerania who underwent MRCP and found that the prevalence of pancreatic cysts significantly increased with age [10]. Our study yielded results similar to these three studies, as the presence of pancreatic cysts was correlated with age. As pertains to IPMN, Chang *et al.* examined 21,745 asymptomatic individuals who underwent CT scans during a health screening examination and reported that the prevalence of IPMN increased with age [9]. This study had a large sample size. Ricci *et al.* screened for IPMNs using abdominal US in outpatients with detected diseases and confirmed their diagnosis using MRCP. The prevalence of IPMNs increased in individuals aged over 50 (OR 3.2; $I<0.001$) and 70 years (OR 1.9; $p<0.001$) [9]. In these two studies, the risk factor associated with IPMNs was age, which was consistent with the findings of our study. Additionally, in a study by Ricci *et al.*, the female sex was positively associated with the presence of IPMNs (OR 1.9; $p<0.001$) [11], which was not examined in our study. We identified other factors associated with IPMN. The presence of high BMI, history of smoking, and the presence of HL, HT, and MS affected the age-related increase in IPMNs.

Obesity may be associated with an increased risk of developing neoplasms in multiple organs, such as pancreatic and colorectal cancer [13, 14]. Current mechanisms by which obesity is postulated to promote cancer include: (1) increased levels and bioavailability of growth factors such as insulin and insulin-like growth factor (IGF-1); (2) increased sex steroid hormones such as estrogen and factors affecting their metabolism; (3) altered adipocytokine levels, such as leptin, adiponectin, and visfatin, which are known to have growth, immune, and tumor-regulatory functions; (4) low-grade inflammation and oxidative stress affecting growth-promoting cytokines and immune modulation; and more recently, (5) altered microbiomes, especially those comprising the intestinal flora [14]. Moreover, recent research has revealed that metabolic diseases such as obesity and type 2 diabetes contribute to pancreatic cancer development through altered metabolic pathways [17, 18]. In the present study, the factors involved in obesity, such as BMI and MS, may be linked to age-related increases in IPMNs through a mechanism similar to that of cancer. These results suggest a potential preventive effect of IPMN onset by improving obesity and metabolic syndrome.

Advances in diagnostic imaging technology, such as CT and MRI, have enabled the increased detection of IPMNs in the pancreas. A proportion of IPMNs evolve over time and can become malignant. Additionally, patients with IPMN are at increased risk of developing conventional PDAC elsewhere in the gland [8, 15, 19]. Our recent study showed that multiple cyst-existing regions (two or more regions) correlated with the incidence of PDAC concomitant with IPMNs (PDAC concomitant with IPMNs in one region vs. two or more regions) [12]. Thus, screening for IPMNs may lead to early detection of pancreatic cancer. However, the use of CT or MRCP for screening is both invasive and expensive. Therefore, alternative screening methods are needed. In the

present study, although the detection rate of IPMNs was lower than that in previous studies using CT or MRI, US remains an ideal tool for screening during medical examinations. In fact, one subject found to have multiple IPMNs was subsequently diagnosed with pancreatic cancer during follow-up and underwent appropriate surgery. Additionally, focusing on cases at high risk for IPMNs may be important. In our study, among elderly subjects with a high BMI, a history of smoking, HL, HT, and MS was associated with a high frequency of IPMNs.

This study has some limitations. First, this was a retrospective cross-sectional study. Prospective cohort studies are required to confirm these results. However, our study included a large cohort of more than 9,000 cases, and there have been few reports based on such a large sample size. Second, 198 patients with pancreatic cysts underwent US at a medical checkup, but none of them underwent further examinations such as CT or MRI. There appears to be a limitation in accurately detecting pancreatic lesions by ultrasonography alone, especially those at the tail or small in size. However, after sampling 303 “pancreatic cyst absent” cases, the results indicated that approximately 5% of cases had existing cysts, while 95% were likely to have no cysts. Therefore, the ability to detect pancreatic lesions on US, although not accurate, seems acceptable. Finally, because this study targeted patients undergoing medical checkups, the number of subjects aged above 70 years was relatively low.

In conclusion, this study found that the prevalence of IPMN increases with age. In addition, lifestyle-related diseases such as MS are associated with an increased prevalence of IPMNs in middle-aged individuals. Hence, it is important to consider age and comorbidities when screening for IPMN.

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Figure legends

Figure 1: Flowchart of study participants

Figure 2: Prevalence of pancreatic cyst and IPMN according to age

Figure 3: Influence of comorbidities and patient characteristics on the frequency of IPMN in the different age groups

Fig 1. Flowchart of subject selection for the analysis

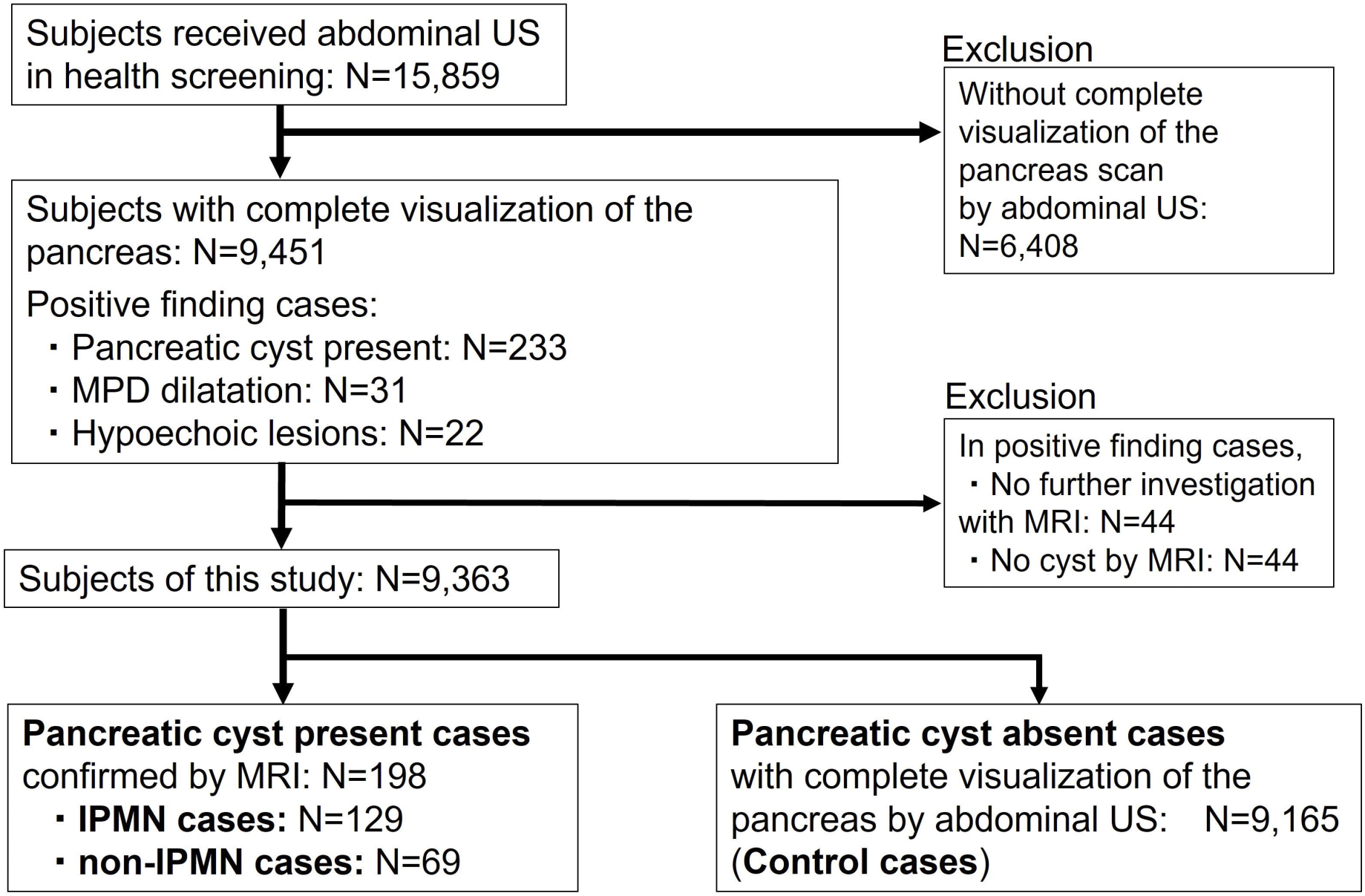
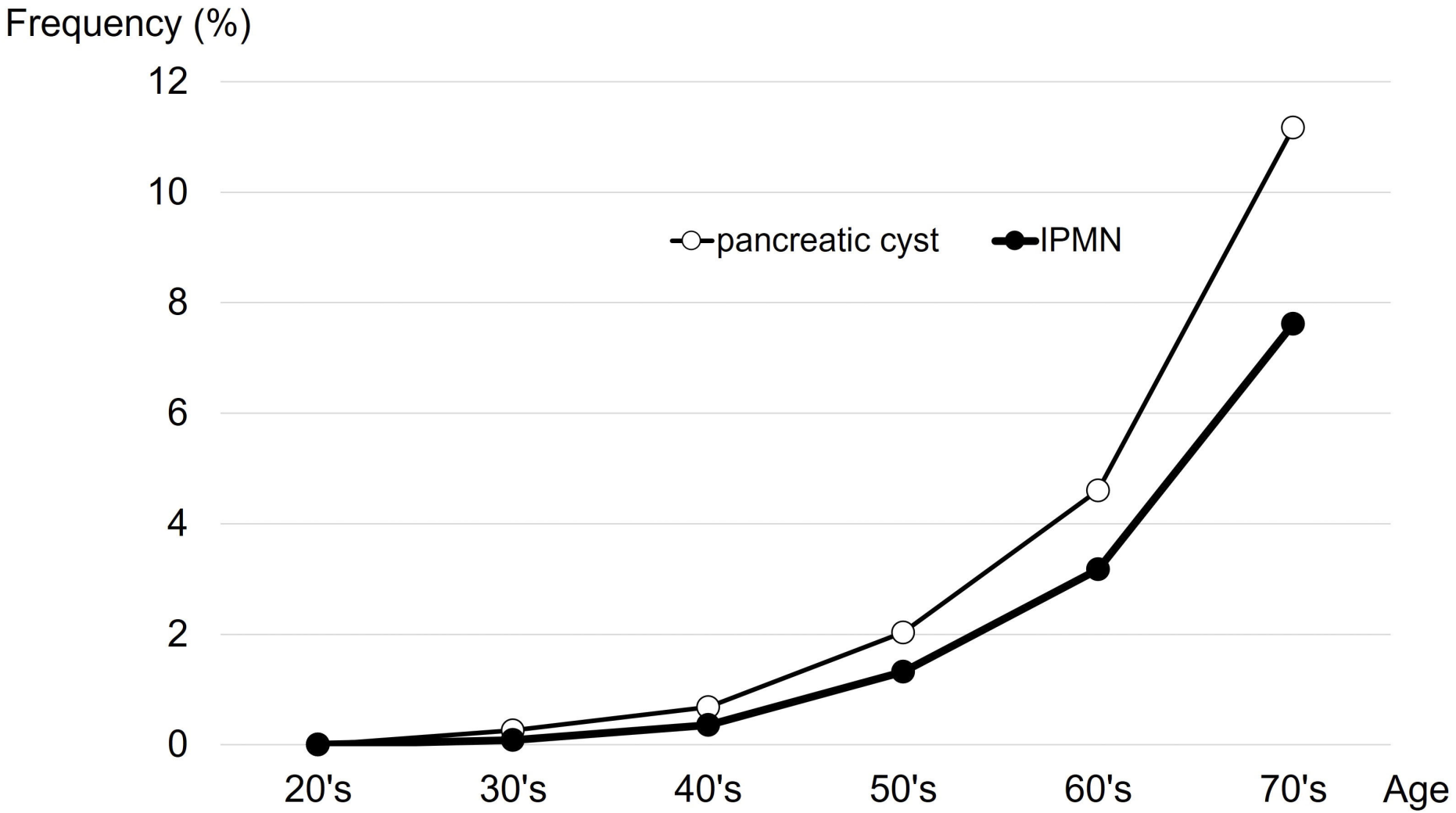


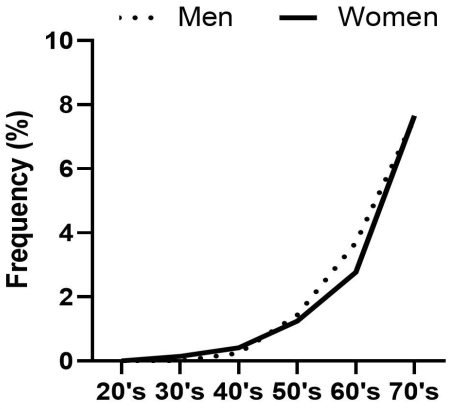
Fig 2. Frequency of pancreatic cyst and IPMN according to age



	20's	30's	40's	50's	60's	70's
Total	72	1163	3385	2806	1543	394
Pancreatic cyst	0	3	23	57	71	44
IPMN	0	1	12	37	49	30

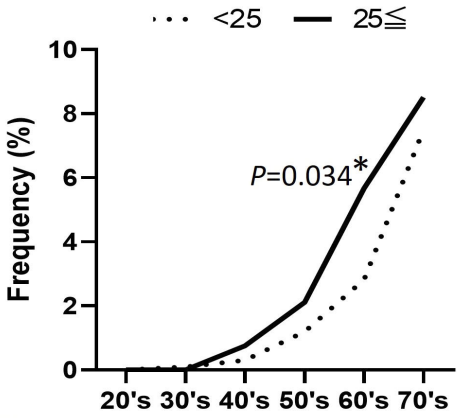
Fig 3. Frequency of IPMN according to age stratified by clinical characteristics

Sex



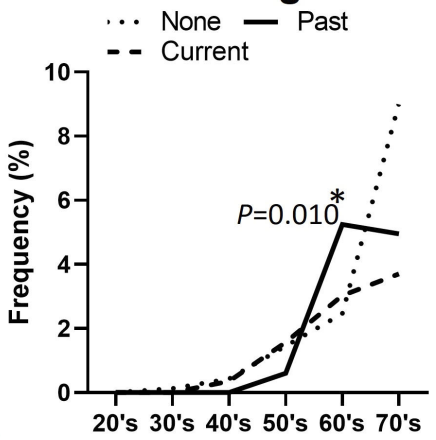
Men						
Total	35	477	1213	1044	677	185
IPMN	0	0	3	15	25	14
Women						
Total	37	686	2172	1762	866	209
IPMN	0	1	9	22	24	16

BMI



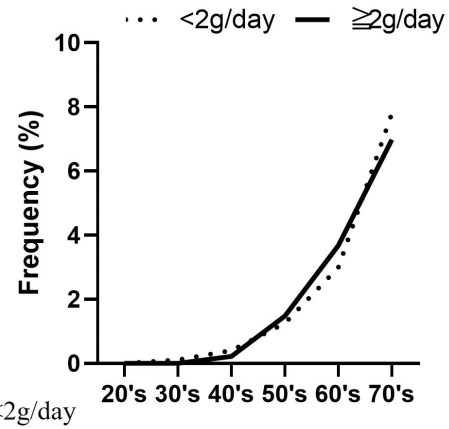
<25						
Total	70	1052	2986	2428	1349	347
IPMN	0	1	9	29	38	26
25≦						
Total	2	111	399	378	194	47
IPMN	0	0	3	8	11	4

Smoking status



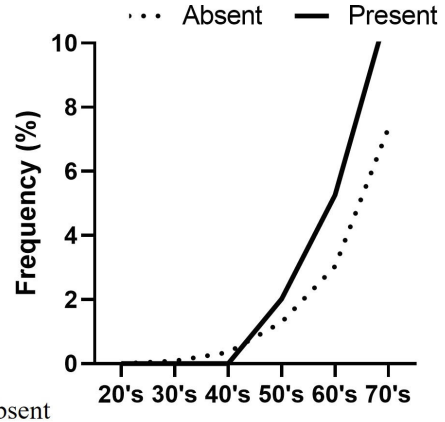
None						
Total	55	771	2328	1925	1016	266
IPMN	0	1	10	28	25	24
Past						
Total	5	192	497	500	362	101
IPMN	0	0	0	3	19	5
Current						
Total	12	200	560	381	165	27
IPMN	0	0	2	6	5	1

Alcohol



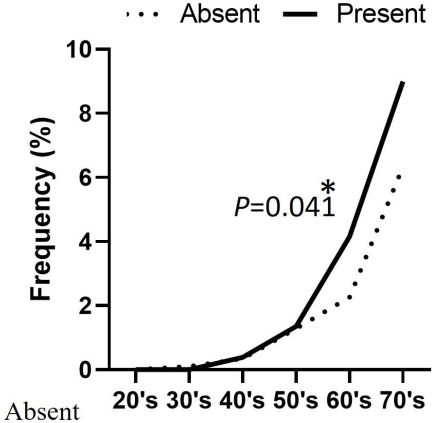
<2g/day						
Total	62	912	2494	1994	1135	308
IPMN	0	1	10	25	34	24
≧2g/day						
Total	10	251	891	812	408	86
IPMN	0	0	2	12	15	6

Diabetes



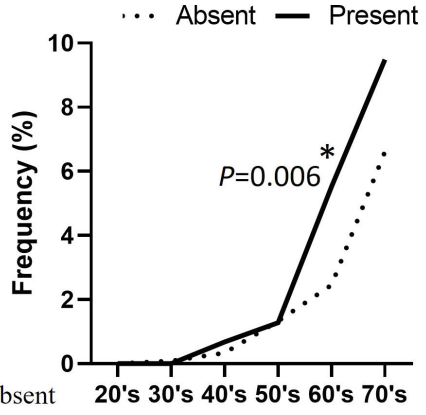
Absent						
Total	72	1159	3351	2707	1448	367
IPMN	0	1	12	35	44	27
Present						
Total	0	4	34	99	95	27
IPMN	0	0	0	2	5	3

Hyperlipidemia



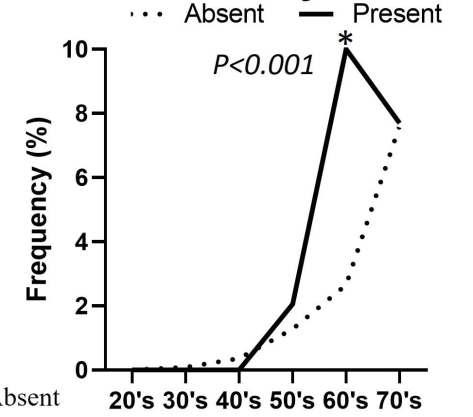
Absent						
total	60	954	2609	1628	797	205
IPMN	0	1	9	21	18	13
Present						
Total	12	209	776	1178	746	189
IPMN	0	0	3	16	31	17

Hypertension



Absent						
Total	72	1151	3238	2414	1181	257
IPMN	0	1	11	32	29	17
Present						
Total	0	12	147	392	362	137
IPMN	0	0	1	5	20	13

Metabolic syndrome



Absent						
Total	72	1152	3309	2660	1433	368
IPMN	0	1	12	34	38	28
Present						
Total	0	11	76	146	110	26
IPMN	0	0	0	3	11	2

Table 1. Characteristics of subjects according to the presence or absence of pancreatic cyst

	Total number	Pancreatic cyst present cases	Pancreatic cyst absent cases	p-value
All patients	9363	198	9165	
Mean age ± SD (years)	50.6 ± 10.2	61.4 ± 10.3	50.4 ± 10.2	<0.001
Sex				0.130
Men	3631 (38.8%)	87 (43.9%)	3544 (38.7%)	
Women	5732 (61.2%)	111 (56.1%)	5621 (61.3%)	
BMI (kg/m^2)				0.120
≥25	1131 (12.1%)	31 (15.7%)	1100 (12.0%)	
<25	8232 (87.9%)	167 (84.3%)	8065 (88.0%)	
Smoking status				0.230
Never	6361 (67.9%)	132 (66.7%)	6229 (66.7%)	
Former	1657 (17.7%)	43 (21.7%)	1614 (17.7%)	
Current	1345 (14.4%)	23 (11.6%)	1322 (14.4%)	

Alcohol consumption				0.750
≥20 g/day	2458 (26.3%)	50 (25.3%)	2408 (26.3%)	
<20 g/day	6905 (73.8%)	148 (73.7%)	6757 (73.7%)	
Hypertension				<0.001
Presence	1050 (11.2%)	54 (27.3%)	996 (10.9%)	
Absence	8313 (88.8%)	144 (72.7%)	8169 (89.1%)	
Hyperlipidemia				<0.001
Presence	3110 (33.2%)	90 (45.4%)	3020 (33.0 %)	
Absence	6253 (66.8%)	108 (54.6%)	6145 (67.0%)	
Diabetes				<0.001
Presence	259 (2.8%)	15 (7.6%)	244 (2.7%)	
Absence	9104 (97.2%)	183 (92.4%)	8921 (97.3%)	
Metabolic syndrome				0.001
Presence	369 (3.9%)	18 (9.1%)	351 (3.8%)	

Absence	8994 (96.1%)	180 (90.9%)	8814 (96.2%)

(%) indicates the proportion of cases with specific clinical features of pancreatic cyst.

BMI, body mass index

Table 2. Logistic regression analysis of risk factors of pancreatic cyst

All participants (n=9, 363)	Univariate analysis		Multivariate analysis*	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (10-year increments)	2.71 (2.36–3.12)	<0.001	2.58 (2.23-2.99)	<0.001
Hypertension (presence)	3.08 (2.22–4.21)	<0.001	1.37 (0.96-1.91)	0.080
Hyperlipidemia (presence)	1.70 (1.28–2.25)	<0.001	1.07 (0.80- 1.43)	0.640
Diabetes (presence)	2.99 (1.67–4.98)	<0.001	1.57 (0.87- 2.67)	0.130

The risk of pancreatic cysts was evaluated according to age, sex, body mass index, smoking status, alcohol consumption. presence of hypertension, presence of hyperlipidemia, and presence of diabetes.

*The odds ratio was adjusted for age and the presence of hypertension, hyperlipidemia, and diabetes.

BMI, body mass index; CI, confidence interval; OR, odds ratio.

Table 3. Logistic regression analysis of risk factors of IPMN cases and non-IPMN cases

IPMN cases (n=129)	Univariable analysis		Multivariable analysis*	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (10-year increments)	2.90 (2.45–3.46)	<0.001	2.73 (2.28–3.29)	<0.001
BMI ≥25 kg/m_2 (presence)	1.85 (1.17–2.81)	0.009	1.53 (0.95–2.41)	0.080
Hypertension (presence)	3.55 (2.40–5.16)	<0.001	1.42 (0.94–2.14)	0.100
Hyperlipidemia (presence)	2.19 (1.55–3.12)	<0.001	1.30 (0.91–1.87)	0.150
Diabetes (presence)	3.07 (1.49–5.64)	0.004	1.41 (0.91–1.87)	0.340
Non-IPMN cases (n=69)	Univariate analysis		Multivariate analysis**	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (10-year increments)	2.41 (1.92–3.01)	<0.001	2.36 (1.87–2.99)	<0.001
Hypertension (presence)	2.28 (1.24–3.95)	0.010	1.08 (0.57–1.94)	0.790
Diabetes (presence)	2.86 (0.99–6.49)	0.051	1.65 (0.57–1.93)	0.320

The risk of pancreatic cysts was evaluated according to age, sex, body mass index, smoking status, alcohol consumption. presence of hypertension, presence of hyperlipidemia, presence of diabetes.

*The odds ratio was adjusted for age, BMI, presence of hypertension, hyperlipidemia, and diabetes.

**The odds ratio was adjusted for age, presence of hypertension, and presence of diabetes.

BMI, body mass index; CI, confidence interval; OR, odds ratio.

Table 4. Morphologic characteristics of IPMN and non-IPMN

	IPMN cases (n=129)	non-IPMN cases (n=69)	p-value
Cyst size (mm)	12.6 ± 7.8	8.5 ± 7.8	<0.001
Multilocular cyst			<0.001
Presence	83 (64.3%)	0 (0.0%)	
Absence	46 (35.7%)	69 (100.0%)	
Communication to main pancreatic duct			<0.001
Presence	76 (58.9%)	0 (0.0%)	
Absence	53 (41.1%)	69 (100.0%)	
Main pancreatic duct dilatation			0.580
Presence	8 (6.2%)	3 (4.4%)	
Absence	121 (93.8%)	66 (95.6%)	
Mural nodule in the cyst			0.300

Presence	2 (1.6%)	0 (0.0%)	
Absence	127 (98.4%)	69 (100.0%)	
Multiple cysts			0.290
Presence	49 (38.0%)	21 (30.4%)	
Absence	80 (62.0%)	48 (69.6%)	

Table 5. Logistic regression analysis of risk factors of pancreatic cyst in their 60s

Age 60 – 69 years (n=1,543)	Univariate analysis		Multivariate analysis*	
	OR (95% CI)	p-value	OR (95% CI)	p-value
BMI > 25 kg/m_2	2.07 (1.04–4.13)	0.034	1.06 (0.46–2.47)	0.887
Smoking Status (past or current smoker)	1.89 (1.07–3.35)	0.032	1.52 (0.83–2.77)	0.176
Hyperlipidemia (presence)	1.88 (1.04–3.38)	0.041	1.57 (0.85–2.88)	0.150
Hypertension (presence)	2.32 (1.30–4.16)	0.006	1.76 (0.93–3.32)	0.080
Metabolic Syndrome (presence)	4.08 (2.02–8.23)	<0.001	3.14 (1.47–6.72)	0.003

*The risk of pancreatic cysts was initially adjusted for age, sex, body mass index, smoking status, and alcohol consumption.

BMI, body mass index; CI, confidence interval; OR, odds ratio.