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【 ORIGINAL ARTICLE 】

A Novel Scoring System to Improve the Detection Efficiency of Pancreatic Cystic Lesions in the General Population

Hiroki Tanaka, Shimpei Matsusaki, Hiroki Asakawa, Satomi Tsuruga, Kenji Nose, Hiroaki Kumazawa, Takashi Sakuno, Yoshiaki Isono, Tomohiro Sase, Hiroshi Okano, Tomonori Saito, Katsumi Mukai and Akira Nishimura

Abstract:

Objective Pancreatic cystic lesions (PCLs) are known risk factors for pancreatic cancer. Therefore, this study explored the predictors identifying PCLs in a general population and developed a scoring system to help more efficiently diagnose these entities during medical checkups.

Methods We reviewed 9,369 examinees of abdominal ultrasound (AUS) during medical checkups between January 2013 and November 2019. Predictors of PCLs were identified using a multivariate logistic regression analysis, and we constructed a scoring system based on these predictors.

Results PCLs were detected in 118 (1.3%). Age 50-59 years old [odds ratio (OR) 2.52, 95% confidence interval (CI) 1.18-5.35], 60-69 years old (OR 3.91, 95% CI 1.86-8.26), and ≥70 years old (OR 10.5, 95% CI 5.03-21.7) as well as abdominal pain (OR 1.85, 95% CI 1.14-3.00), alcohol consumption (OR 1.72, 95% CI 1.03-2.89), a family history of pancreatic cancer (OR 2.41, 95% CI 1.09-5.34), and pre-diabetes or diabetes (OR 1.78, 95% CI 1.05-3.00) were predictors of PCLs. The following scores were assigned according to regression coefficients: age (50-59 years old, 1 point; 60-69 years old, 1.5 points; ≥70 years old, 2.5 points); abdominal pain, 1 point, alcohol consumption, 1 point; a family history of pancreatic cancer, 1 point; and pre-diabetes, 1 point. The PCL detection rate increased with the total score: 0.2% for total score 0 point, 5.4% for ≥4.0 points. The area under the curve of the scoring system was 0.75 (95% CI 0.70-0.79).

Conclusion Our scoring system allows the risk of PCLs to be determined and may help more efficiently diagnose these entities.

Key words: abdominal ultrasound, general population, pancreatic cystic lesions, scoring system

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Introduction

Pancreatic cancer is known to have a poor prognosis, with patients with resectable disease accounting for approximately 20% of all patients with pancreatic cancer (1, 2). Many efforts are being made to enable the early detection of pancreatic cancer. Abdominal ultrasound (AUS) is a noninvasive imaging examination that is often performed at a medical checkup. The indirect findings of AUS, such as pancreatic duct dilatation and pancreatic cysts, as well as the detection of the mass lesion itself, are useful in the diagnosis of pancreatic cancer (3-5). However, the detection rate of pancreatic cancer with screening AUS alone is not markedly different from the incidence of pancreatic cancer in Japan (33.5 in 100,000 people) (6, 7). This may be because medical checkup examinees tend to be younger than patients with pancreatic cancer and AUS sometimes cannot visualize the entire pancreas. While it may be difficult to detect pancreatic cancer with screening AUS alone, AUS for cancer screening is important for not only detecting pancreatic cancer but also identifying high-risk individuals (HRIs) for pan-

Department of Gastroenterology, Suzuka General Hospital, Japan
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Correspondence to Dr. Hiroki Tanaka, hiroki.tanaka@miekosei.or.jp

creatic cancer. Pancreatic cystic lesions (PCLs) including intrapapillary mucinous neoplasms (IPMNs) are known risk factors for pancreatic cancer. Surveillance for PCLs is important for the early detection of pancreatic cancer (8-12). However, most patients with PCLs are asymptomatic and PCLs are often not recognized before the diagnosis of pancreatic cancer. A previous study in our hospital reviewing imaging studies at the diagnosis of pancreatic cancer from our hospital showed that 17.5% (43/246) of patients with pancreatic cancer had coexisting PCLs (13). In contrast, only 18.6% (8/43) of these PCLs were recognized before the diagnosis of pancreatic cancer. PCLs are not thus sufficiently identified prior to the diagnosis of pancreatic cancer, underscoring the need for the more efficient detection of PCLs. In the present study, we explored the predictors of PCL detected on AUS at a medical checkup and developed a scoring system to help more efficiently diagnose these entities.

Materials and Methods

Subjects

Subjects who underwent AUS during a medical checkup between January 2013 and November 2019 were enrolled in this study. Information, such as the medical history, family history, and history of smoking and alcohol consumption was obtained from the medical questionnaire at the time of the medical checkup. AUS was performed using a LOGIQ E9 (GE Healthcare, Chicago, USA), Aplio500 (Canon Medical Systems, Otawara, Japan), and ProSound α10 (Hitachi Aloka Medical, Tokyo, Japan). When PCLs were suspected on AUS, examinees were recommended to undergo further examinations with contrast-enhanced computed tomography, magnetic resonance cholangiopancreatography (MRCP), or endoscopic ultrasonography (EUS). Examinees with PCLs were defined as those with cysts confirmed by further examinations, and those who were suspected of having PCLs on AUS but did not undergo further examinations were excluded from this study. Examinees with PCLs were surveilled with MRCP or EUS every 6-12 months. We divided AUS examinees into two groups according to the presence or absence of PCLs and retrospectively analyzed the clinical features of the examinees, including risk factors for pancreatic cancer. Each factor was defined as follows: diabetes, defined as a history of diabetes or hemoglobin A1c (HbA1c) ≥ 6.5%; pre-diabetes, defined as HbA1c ≥5.7%; smoking, defined as smoking at least 100 cigarettes in a lifetime; alcohol consumption, defined as drinking ≥37.5 g/day of alcohol; a family history of pancreatic cancer, defined as at least one first-degree relative with pancreatic cancer; and obesity, defined as a body mass index (BMI) ≥30 kg/m^2. Abdominal pain was defined in cases with symptoms that occurred within one month prior to the medical checkup and were noted on the medical questionnaire at the time of the medical checkup. This study was performed with institutional review board approval (Suzuka General Hospital, approval number 230). The requirement for a written informed consent was waived because this was a retrospective study using de-identified data.

Statistical analyses

Continuous variables are expressed as the median and interquartile range (IQR), and categorical variables are expressed as the number and frequency (%) of observations. Univariate and multivariate logistic regression analyses were performed to evaluate the predictors of PCLs. A goodness-of-fit test for the model was performed using the Hosmer-Lemeshow test. Thereafter, we constructed a scoring system according to the predictors of PCLs. Point values were assigned to each case based on the coefficients of each predictor that showed significance in bootstrapping (1,000 simulations) in a multivariate logistic regression analysis (14). The coefficients of each predictor were rounded up to the nearest 0.5. We evaluated the detection rate of PCLs for each total point value. The usefulness of the scoring system was assessed by the area under the receiver operating characteristic curve (AUC) and the Cochran-Armitage test. The detection rate of PCLs based on the scoring system was validated using bootstrapping with 1,000 simulations. Statistical analyses were conducted using the SPSS Statistics software program, version 25.0 (IBM, Armonk, USA), and EZR version 1.54 (15), with a p value of <0.05 was considered statistically significant.

Results

Characteristics of AUS examinees

We reviewed 9,403 examinees who underwent AUS during a medical checkup at our hospital. Of them, 34 examinees who were suspected of having PCLs on AUS but did not undergo further examinations were excluded. Thus, the remaining 9,369 examinees were enrolled in this study (Fig. 1). Of the examinees, 118 (1.3%) were eventually diagnosed with PCLs (99 branch-duct IPMNs, 1 mixed-type IPMN, and 18 simple cysts or indeterminate cystic lesions). None of the examinees showed invasive IPMNs or IPMNs with worrisome features or high-risk stigmata based on the Fukuoka guidelines (16). Table 1 shows the characteristics of the 9,369 examinees enrolled in this study. The median age of the examinees was 54 (IQR 44-62) years old, which was younger than the patients with pancreatic cancer (n= 246, median 74 years old, IQR 69-82 years old) diagnosed at our hospital during the same period (Fig. 2). Pancreatic cancer was diagnosed in 4 of the 118 examinees with PCLs (Fig. 3). All four patients had resectable pancreatic cancer concomitant with IPMNs, and pancreatic cancer was diagnosed using regular imaging examinations for PCLs (Table 2). Six cases of pancreatic cancer were diagnosed during the study period in 9,251 examinees without PCLs.

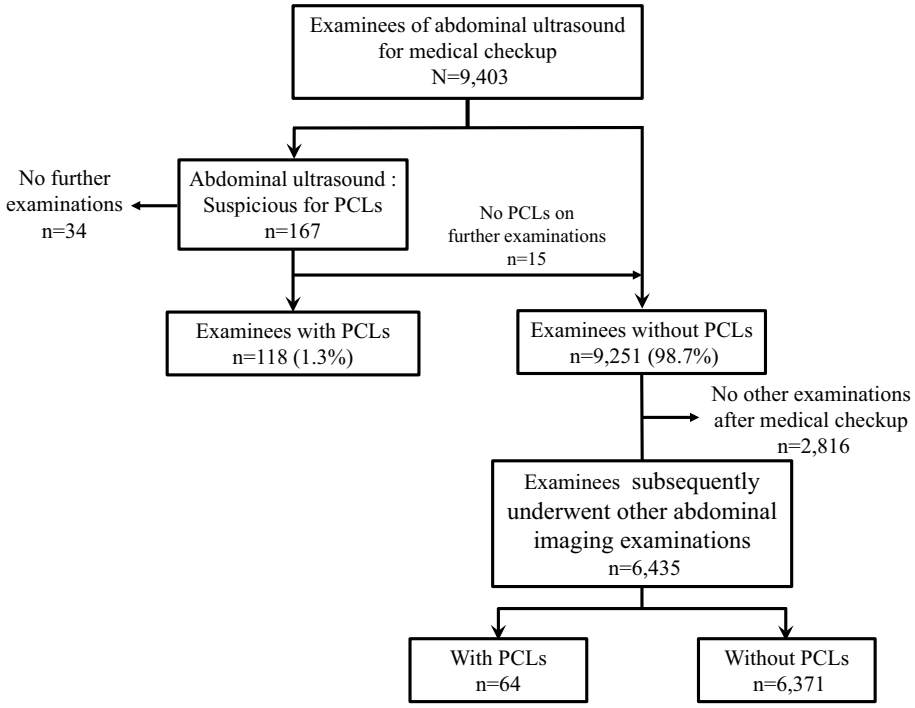

Figure 1. Subject enrollment. A total of 9,403 examinees who underwent abdominal ultrasound at a medical checkup were enrolled in this study. Of them, 34 were excluded, and the remaining 9,369 examinees were reviewed. Of the examinees, 118 (1.3%) were eventually diagnosed with pancreatic cystic lesions.

Table 1. The Characteristics of Examinees of Abdominal Ultrasound for Medical Checkup.

	Examinees with pancreatic cystic lesions n=118		Examinees without pancreatic cystic lesions n=9,251	
Men: women	61:57	51.7%	5,511:3,740	59.6%
Age (years), median (IQR)	65 (57-72)		54 (44-62)	
Abdominal pain	24/118	20.3%	1,137/9,251	12.3%
HbA1c (%), median (IQR)	6 (5.8-6.3)		5.7 (5.5-6.0)	
Diabetes	19/118	16.1%	958/9,251	10.4%
Pre-diabetes or diabetes	90/118	76.3%	4,946/9,251	53.5%
Smoking	49/118	41.5%	4,401/9,251	47.6%
Alcohol consumption	25/118	21.2%	1,414/9,251	15.3%
Obesity	2/118	1.7%	444/9,251	4.8%
Family history of pancreatic cancer	7/118	5.9%	211/9,251	2.3%
Amylase (IU/mL), median (IQR)	95 (70-111)		80 (64-100)	
Amylase ≥137 IU/mL	14/114	12.3%	586/9,092	6.4%

HbA1c: hemoglobin A1c, IQR: interquartile range

Predictors of PCLs

Table 3 shows the results of univariate and multivariate logistic regression analyses. A multivariate logistic regression analysis revealed that age 50-59 years old [odds ratio (OR) 2.52, 95% confidence interval (CI) 1.18-5.35, p=0.017], 60-69 years old (OR 3.91, 95% CI 1.86-8.26, p<0.001), and ≥70 years old (OR 10.5, 95% CI 5.03-21.7, p<0.001); abdominal pain (OR 1.85, 95% CI 1.14-3.00, p=0.013); alcohol consumption (OR 1.72, 95% CI 1.03-2.89, p=0.040); a family history of pancreatic cancer (first-degree relatives) (OR 2.41, 95% CI 1.09-5.34, p=0.030); and pre-diabetes or diabetes (OR 1.78, 95% CI 1.05-3.00, p=0.032) were predictors of PCLs. The Hosmer-Lemeshow test showed the following results: chi-square value=2.04, degrees of freedom=8, and p=0.980.

Scoring system for PCLs

The following scores were assigned to the predictors of PCLs that were significantly different in bootstrapping in the

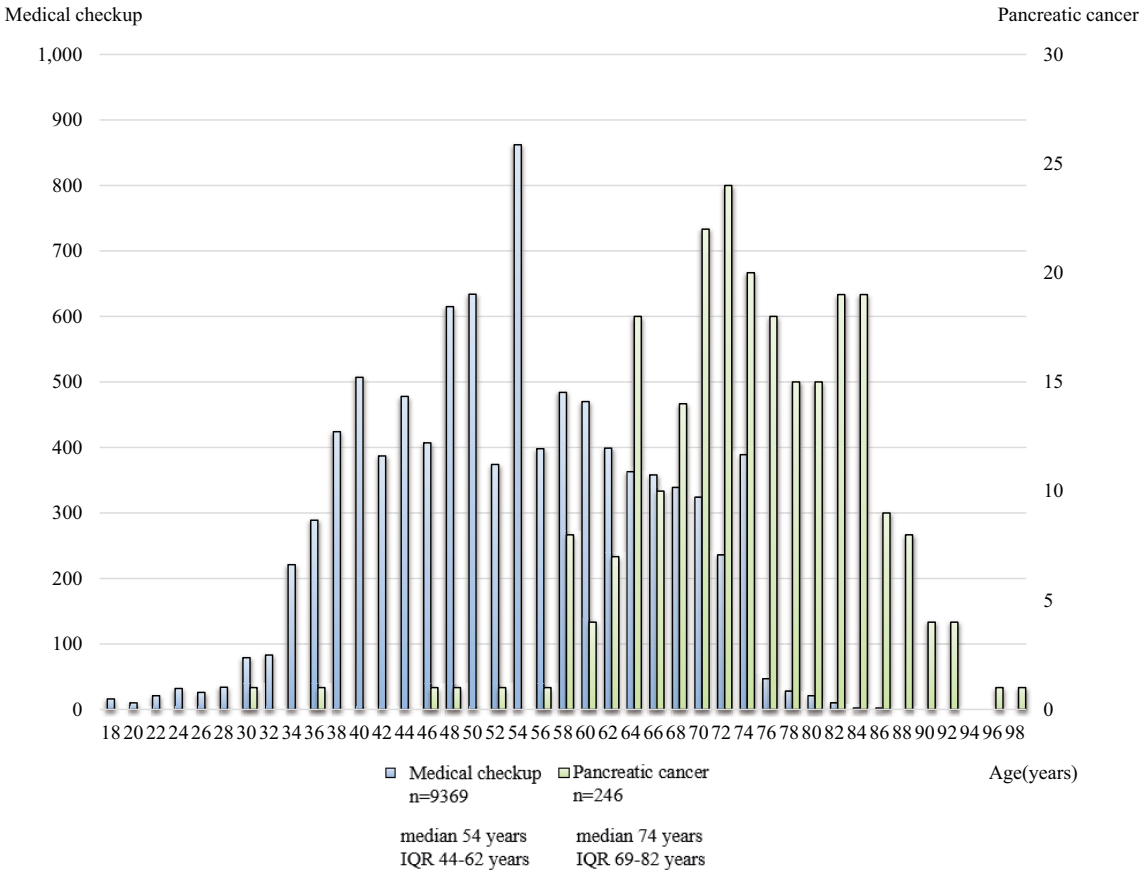

Figure 2. **Age distribution of cancer screening examinees and pancreatic cancer patients. The median age of the cancer screening examinees was 54 years old, which was younger than the patients with pancreatic cancer (median 74 years old) diagnosed at our hospital during the same period.**

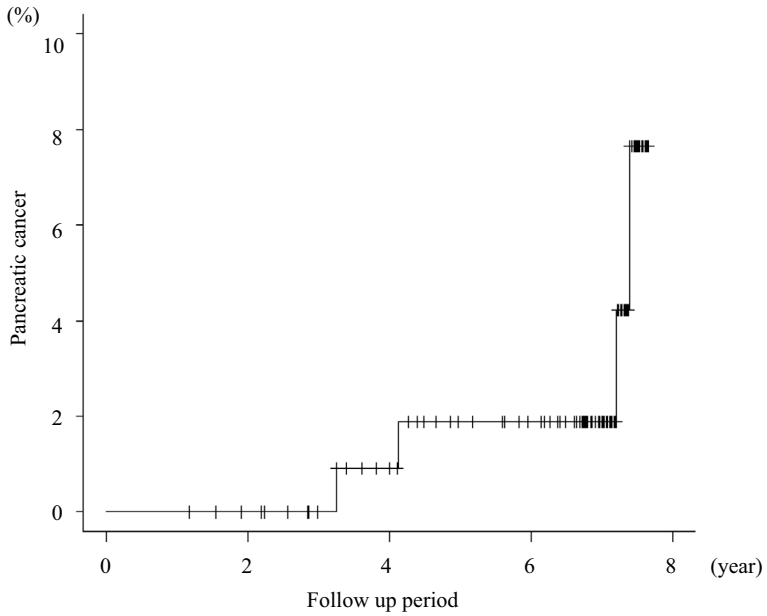

Figure 3. **The frequency of pancreatic cancer among the abdominal ultrasound examinees.**

multivariate analysis, according to regression coefficients: age (50-59 years old, 1.0 point; 60-69 years old, 1.5 points; ≥70 years old, 2.5 points); abdominal pain, 1.0 point; alcohol consumption, 1.0 point; a family history of pancreatic cancer, 1.0 point; and pre-diabetes or diabetes, 1.0 point (Table 3). The detection rate of PCLs was 0.2% [n/N=3/1,828, Boot strapping bias-corrected and accelerated (BCa) 95% CI 0.1-0.3%] for a total score of 0 points, 0.5% (n/N=

Table 2. Clinical Features of Patients Diagnosed with Pancreatic Cancer among Those with or without PSLs on Medical Checkup.

Case	Age*	Sex	PCLs detected in AUS for medical checkup	Opportunity for diagnosis of pancreatic cancer	Duration from medical checkup to diagnosis of pancreatic cancer	Tumor size (mm)	Resectability*	Stage**	Prognosis
1	74	M	Presence	Surveillance for IPMN	39.6 months	NA†	R	NA†	No recurrence 14 months after surgery
2	76	W	Presence	Surveillance for IPMN	89.9 months	15	R	IIA	No recurrence 21 months after surgery
3	74	M	Presence	Surveillance for IPMN	50.2 months	45††	R	IIB	Dead 29 months after diagnosis
4	71	M	Presence	Surveillance for IPMN	87.8 months	25	R	IIB	No recurrence 23 months after surgery
5	73	M	Absence	AUS Constant medical checkup	24.6 months	15	R	IIA	No recurrence 83 months after surgery
6	71	M	Absence	Imaging examination for other diseases	25.8 months	15	R	IIA	No recurrence 38 months after surgery
7	70	W	Absence	Jaundice	61.8 months	30	R	IIA	Dead 2 months after diagnosis
8	80	W	Absence	Abdominal pain	73.8 months	48	R	IIB	No recurrence 30 months after surgery
9	74	M	Absence	Imaging examination for other diseases	67.1 months	17	UR-M	IV	Alive 36 months after diagnosis
10	69	W	Absence	Anemia	2.6 months	36	UR-M	IV	Dead 9 months after diagnosis

PCLs: pancreatic cystic lesions, IPMN: intraductal papillary mucinous neoplasms, AUS: abdominal ultrasound

*NCCN Guidelines Version 1. 2021 Pancreatic Adenocarcinoma.

**TNM Classification of Malignant Tumours, 8th ed.

†Details unknown as the surgery was performed at another hospital.

††Due to lack of consent, the surgery was performed 6 months after the detection of pancreatic cancer.

12/2,278, BCa 95% CI 0.3-0.8%) for 1.0 point, 1.3% (n/N= 5/386, BCa 95% CI 0.8-1.9%) for 1.5 points, 0.8% (n/N= 14/1,752, BCa 95% CI 0.5-1.1%) for 2.0 points, 1.6% (n/N =21/1,274, BCa 95% CI 1.1-2.2%) for 2.5 points, 2.1% (n/N=10/476, BCa 95% CI 1.1-3.2%) for 3.0 points, 3.3% (n/N =34/1,020, BCa 95% CI 2.4-4.6%) for 3.5 points, and 5.4% (n/N=19/355, 3.4-7.6%) for ≥4.0 points, showing an increasing trend with the total score of the scoring system (Cochran-Armitage test, $p<0.001$) (Table 4, Fig. 4). The AUC of the scoring system for PCLs prediction was 0.75 (95% CI 0.70-0.79) (Fig. 5).

PCLs diagnosed by examinations other than AUS for medical checkup

Of the 9,251 examinees whose AUS for medical checkup did not reveal PCLs, 6,435 subsequently underwent other abdominal imaging examinations such as AUS, CT, MRI, and EUS, to investigate other diseases and abdominal symptoms during the study period. Of these, 64 examinees were diagnosed with PCLs (Fig. 1). The PCL detection rate among these examinees also increased with the total score of the scoring system at the time of the medical checkup (Cochran-Armitage test, $p<0.001$) (Fig. 6).

Discussion

The early detection of pancreatic cancer is difficult because most patients with stage I pancreatic cancer are reported to be asymptomatic (17). Therefore, surveillance for pancreatic cancer in HRIs without symptoms is important for the early detection of pancreatic cancer. IPMNs have been recognized as risk factor for pancreatic cancer (8). The incidence rate of pancreatic cancer concomitant with branch-duct IPMNs is reported to be approximately 1% per year (9-12). In addition, pancreatic cysts other than IPMNs are also considered to be risk factors for pancreatic cancer (9). However, PCLs are often not recognized before the diagnosis of pancreatic cancer. In fact, a previous study in our hospital showed that most PCLs were not recognized before the diagnosis of pancreatic cancer (13). Therefore, a more efficient method for detecting PCLs is necessary.

In the current study, the age, family history of pancreatic cancer, presence of pre-diabetes or diabetes, abdominal pain, and alcohol consumption were predictors of PCLs in examinees who underwent AUS for medical checkups. Previous studies have also investigated predictors of PCLs, and some factors have been reported. Of them, age is a well-known

Table 3. Predictors of Pancreatic Cystic Lesions (Univariate and Multivariate Logistic Regression Analyses).

	Univariate analysis		Multivariate analysis		Bootstrapping			Points
	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value	Coefficients mean	BCa 95% CI	p value	
Gender: women	1.38 (0.96-1.98)	0.085	1.55 (0.94-2.56)	0.088	0.44	-0.090-0.98	0.091	
Age <50 years	Reference		Reference					
50-59 years	3.21 (1.64-6.30)	<0.001	2.52 (1.18-5.35)	0.017	0.92	0.19-1.92	0.013	1.0
60-69 years	5.08 (2.61-9.89)	<0.001	3.91 (1.86-8.26)	<0.001	1.37	0.69-2.32	<0.001	1.5
>70 years	13.4 (7.05-25.4)	<0.001	10.5 (5.03-21.7)	<0.001	2.35	1.73-3.41	<0.001	2.5
Abdominal pain	1.82 (1.16-2.87)	0.0093	1.85 (1.14-3.00)	0.013	0.62	0.12-1.02	0.012	1.0
Smoking	0.78 (0.54-1.13)	0.19	0.83 (0.50-1.37)	0.46	-0.19	-0.77-0.39	0.49	
Alcohol consumption	1.49 (0.96-2.33)	0.079	1.72 (1.03-2.89)	0.040	0.54	0.054-1.0	0.027	1.0
Obesity	0.35 (0.085-1.40)	0.14	0.53 (0.13-2.20)	0.39	-0.63	-16.6-0.29	0.20	
Family history of pancreatic cancer	2.73 (1.25-5.92)	0.011	2.41 (1.09-5.34)	0.030	0.88	0.009-1.45	0.015	1.0
Amylase ≥137 IU/mL	2.01 (1.14-3.54)	0.015	1.48 (0.83-2.64)	0.19	0.39	-0.27-0.85	0.20	
Pre-diabetes or diabetes	2.80 (1.74-4.51)	<0.001	1.78 (1.05-3.00)	0.032	0.57	0.077-1.20	0.022	1.0
Diabetes	1.56 (0.95-2.56)	0.082						

BCa: bias-corrected and accelerated, CI: confidence interval

Table 4. Relationship between the Scoring System and the Detection Rate of Pancreatic Cystic Lesions.

Point	Pancreatic cystic lesions		Bootstrapping
	n/N	%	BCa 95% CI (%)
0	3/1,828	0.2%	0.1-0.3%
1	12/2,278	0.5%	0.3-0.8%
1.5	5/386	1.3%	0.8-1.9%
2	14/1,752	0.8%	0.5-1.1%
2.5	21/1,274	1.6%	1.1-2.2%
3	10/476	2.1%	1.1-3.2%
3.5	34/1,020	3.3%	2.4-4.6%
4.0-	19/355	5.4%	3.4-7.6%
Total	118/9,369	1.3%	1.0-1.5%

BCa: bias-corrected and accelerated, CI: confidence interval

predictor of PCLs, and the detection rate of PCLs increases with age (3, 18-21). Furthermore, Soroida et al. reported that gender (women: OR 1.29, p=0.001) as well as age were predictors of PCLs in a study of AUS examinees at medical checkups (20). Ricci et al. also showed that age and gender (women: OR 1.9, p<0.001) were predictors of pancreatic cysts in a study of outpatients who underwent AUS (21). Although not significant, PCLs also tended to be more common in women than men in the present study as well (OR 1.55, 95% CI 0.94-2.56). Capurso et al. compared IPMN patients with age- and sex-adjusted controls and showed that chronic pancreatitis (OR 10.1, 95% CI: 1.30-78.32), a family history of pancreatic cancer (OR 2.94, 95% CI: 1.17-7.39), and diabetes mellitus (OR 1.79, 95% CI: 1.08-2.98), are predictors of PCLs (22). Bartsch et al. performed annual screening with MRI and EUS for 253 individuals at risk of familial pancreatic cancer. Of them, 83 (32.8%) had PCLs at the initial screening, and 43 (17.0%) newly developed PCLs during a median follow-up of 28 (range 3-152) months (23). Pre-diabetes or diabetes was also a stronger predictor of PCLs than diabetes in the present study. Previous studies have suggested that IPMNs cause pancreatic parenchymal atrophy by producing excessive viscous mucin (24, 25). This may be associated with glucose intolerance in IPMN patients. In contrast, diabetes has been reported to be more strongly associated with invasive IPMNs than with noninvasive IPMNs (26, 27). None of the patients in the present study had invasive IPMNs, which may explain why glucose intolerance was relatively unaffected by PCLs. Although there are few studies regarding the relationship between smoking and IPMN, a comparative study of smokers and nonsmokers with IPMN found that smokers were younger than nonsmokers, suggesting an association between smoking and IPMN development (28). The association between IPMNs and other factors, such as abdominal pain and alcohol consumption has rarely been reported and remains unclear. Further investigations will be necessary to evaluate whether or not these factors are useful as predictors of

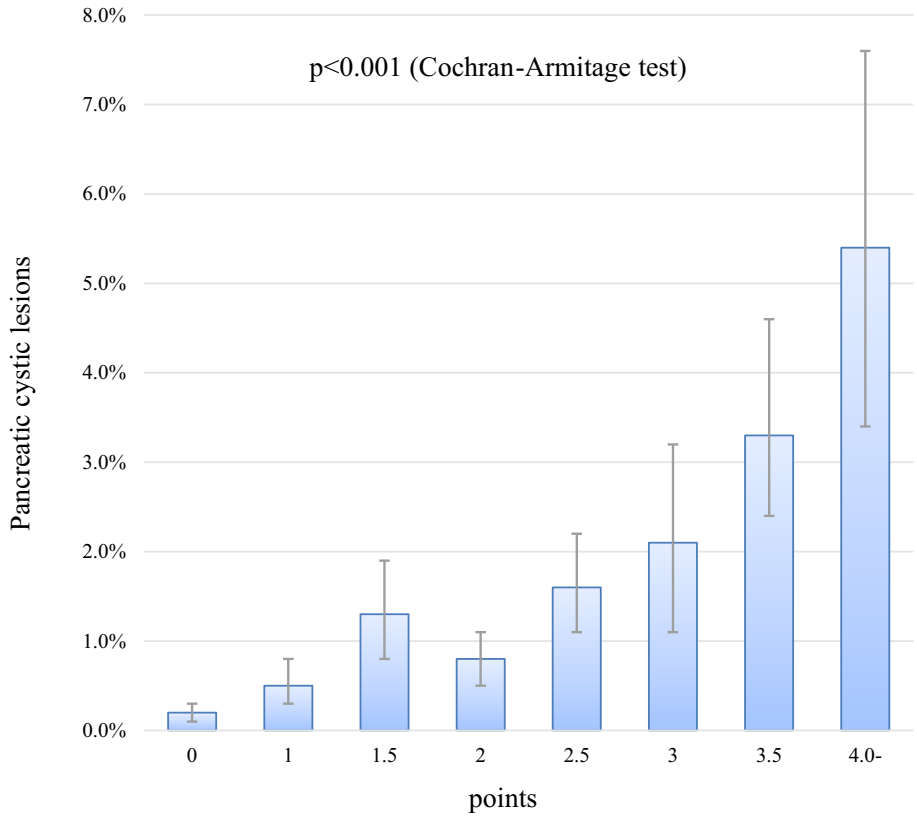

Figure 4. **Relationship between the scoring system and the detection rate of pancreatic cystic lesions. The detection rate of pancreatic cystic lesions (frequencies and BCa 95% CI) increased with the total score of the scoring system. BCa: bias-corrected and accelerated, CI: confidence interval**

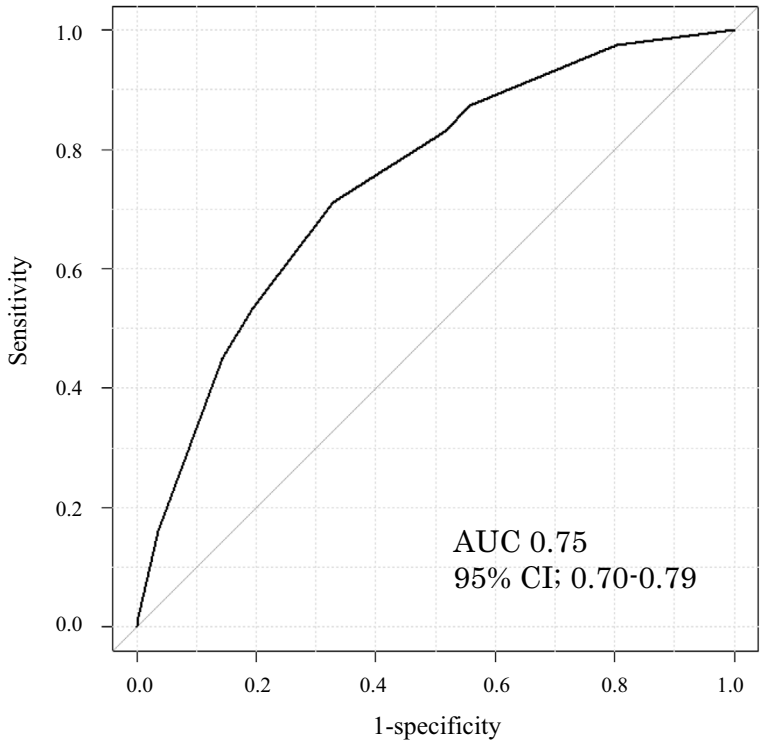

Figure 5. **The AUC of the scoring system for pancreatic cystic lesions prediction. The AUC of the scoring system for PCL prediction was 0.75 (95% CI 0.70-0.79). AUC: area under the receiver operating characteristic curve, CI: confidence interval**

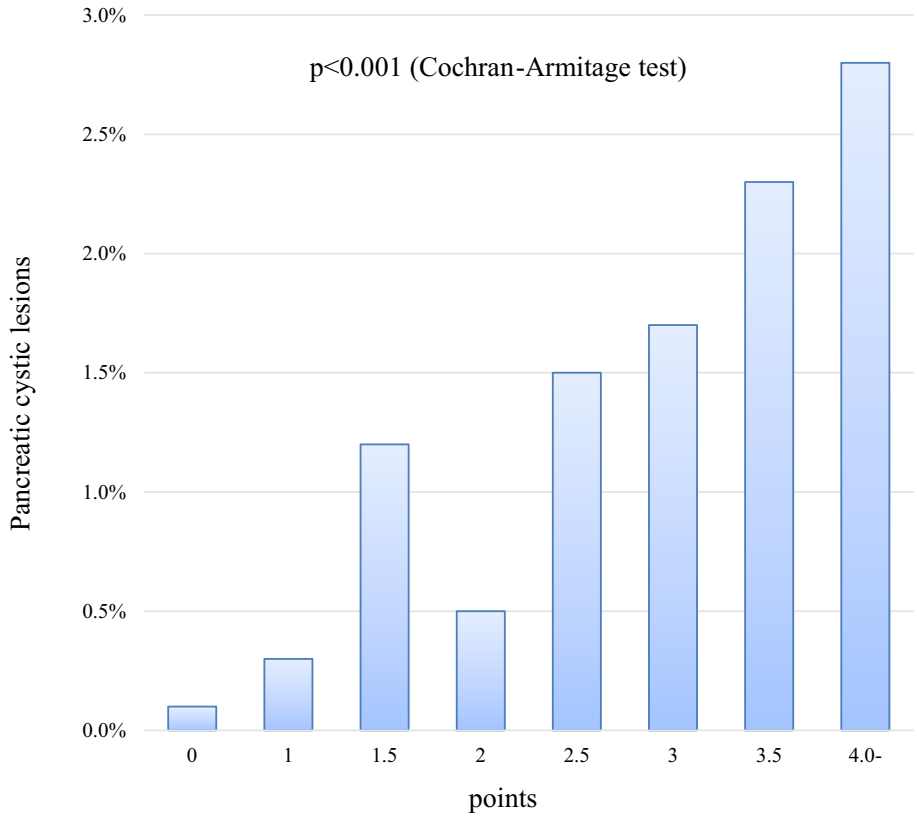

Figure 6. **Relationship between the scoring system and the detection rate of pancreatic cystic lesions among 6,435 examinees who underwent other abdominal imaging examinations after medical checkups. The detection rate of pancreatic cystic lesions also increased with the total score of the scoring system among these examinees.**

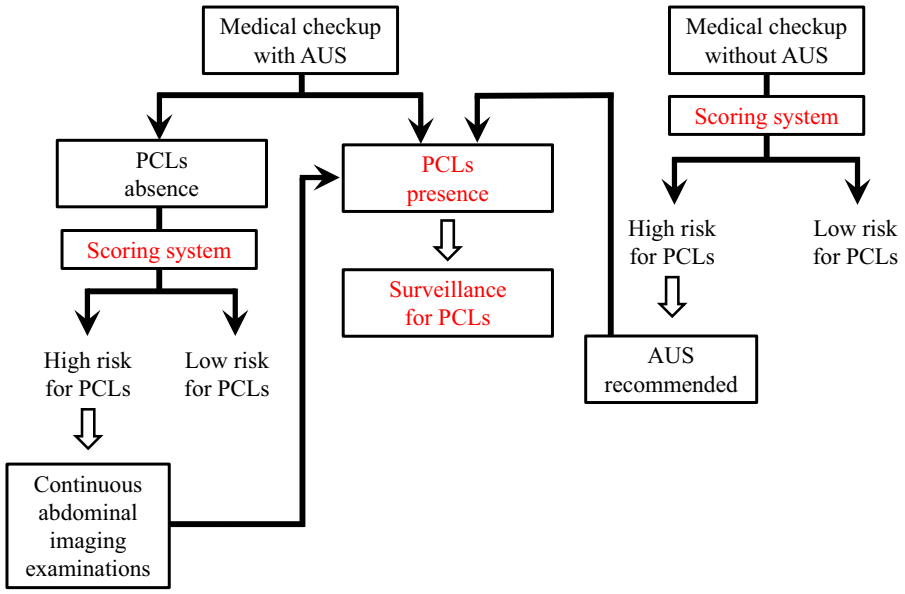

Figure 7. **Our recommendation for the efficient detection of PCLs based on this study.**

PCLs.

The present scoring system based on predictors of PCLs showed that the detection rate of PCLs increased with the total score. We consider the assessment of the risk of PCLs using the scoring system to contribute to improving the detection rate of PCLs in two main ways. First, the ability of AUS to detect PCLs is limited and continuous imaging examinations may be useful in high-risk individuals for PCLs (Fig. 7). In this study, some examinees who underwent other abdominal imaging examinations after medical checkups were diagnosed with PCLs. The detection rate of PCLs among these examinees also increased with the total score

of the scoring system at the time of the medical checkup. These PCLs include those that newly developed after the medical checkup and those that were missed by AUS. Therefore, continuous imaging examinations may be recommended for HRIs of PCLs in the scoring system, even if PCLs are not detected on AUS at the medical checkup. Second, this scoring system may provide a basis for recommending AUS to examinees who have not yet undergone AUS during a medical checkup. There were 4,144 examinees who underwent medical checkups without AUS during this study period, undergoing only simple examinations, such as blood tests. Furthermore, there are many people who do not undergo a medical checkup itself. For subjects who do not receive AUS, AUS is recommended to those at high risk for developing PCLs in order to identify PCLs more efficiently.

Several limitations associated with the present study warrant mention. First, this study was a retrospective case-control study, and not all patients are followed up after their medical checkups. Therefore, it was difficult to determine the exact frequency of PCLs that were subsequently detected after AUS during medical checkup. Either a follow-up survey of subjects who could not be followed up after their medical checkups or a prospective study including a follow-up survey after medical checkups should be performed to mitigate this limitation. Second, we performed internal validation of the scoring system using bootstrapping, however, external validation was absent. The present scoring system was based on simple methods such as medical questionnaire survey and blood tests. However, the relatively low AUC is likely due to the fact that the scoring system is not based on imaging examinations that directly assess PCLs. Furthermore, risk factors for PCLs have not yet been sufficiently clarified. Therefore, the robustness of this scoring system should be evaluated by external validation in a different population in the future. Third, the medical checkup was performed using AUS. MRCP and EUS are superior to AUS for detecting PCLs but are unsuitable for screening, as they are relatively time consuming and EUS is invasive. In contrast, AUS is simple and non-invasive and widely performed for medical checkups. However, AUS sometimes cannot visualize the entire pancreas, and its ability to detect PCLs is limited. Indeed, in the present study, 298 examinees (3.2%) were determined to have an "inadequate pancreatic evaluation by AUS". Furthermore, some examinees were diagnosed with PCLs on imaging studies performed after the medical checkup. Among these cases, some lesions may have developed after the medical checkup, while others may have been missed by AUS. Continuous imaging examinations may be advisable in HRIs of PCLs using the scoring system, even if PCLs are not detected on AUS at the medical checkup.

Conclusion

We introduced a scoring system that helps determine the risk of PCLs using simple methods, such as a medical questionnaire survey and blood tests. Furthermore, the present scoring system may facilitate the more efficient detection of PCLs.

The authors state that they have no Conflict of Interest (COI).

References

1. Ryan DP, Hong TS, Bardeesy N. Pancreatic adenocarcinoma. N Engl J Med **371**: 1039-1049, 2014.
2. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. CA Cancer J Clin **68**: 7-30, 2018.
3. Fujisawa T, Isayama H, Gunji T, et al. Prevalence rate and predictive factors of pancreatic diseases in cases with pancreatic duct dilatation: a cross-sectional study of a large, healthy Japanese population. Intern Med **59**: 769-777, 2020.
4. Hanada K, Okazaki A, Hirano N, et al. Diagnostic strategies for early pancreatic cancer. J Gastroenterol **50**: 147-154, 2015.
5. Sakamoto H, Harada S, Nishioka N, et al. A social program for the early detection of pancreatic cancer: the Kishiwada Katsuragi project. Oncology **93**: 89-97, 2017.
6. Kumada K, Miyashita Y, Horiuchi K, et al. Evaluation and measures of pancreatic cancer screening by ultrasonography in general medical checkups. Health Eval Promot **41**: 259-267, 2014 (in Japanese).
7. Cancer registry and statistics. Cancer Information Service, National Cancer Center, Japan (Ministry of Health, Labour and Welfare, National Cancer Registry) [Internet]. 2018 [updated 2021 Jul 1; cited 2021 Sep 15]. Available from: https://view.officeapps.live.com/op/view.aspx?src=https%3A%2F%2Fganjoho.jp%2Freg_stat%2Fstatistics%2Fdata%2Fdl%2Fexcel%2Fcancer_incidenceNCR(2016-2018)E.xls&wdOrigin=BROWSELINK
8. Tanaka M. Intraductal papillary mucinous neoplasm of the pancreas as the main focus for early detection of pancreatic adenocarcinoma. Pancreas **47**: 544-550, 2018.
9. Oyama H, Tada M, Takagi K, et al. Long-term risk of malignancy in branch-duct intraductal papillary mucinous neoplasms. Gastroenterology **158**: 226-237, 2020.
10. Tada M, Kawabe T, Arizumi M, et al. Pancreatic cancer in patients with pancreatic cystic lesions: a prospective study in 197 patients. Clin Gastroenterol Hepatol **4**: 1265-1270, 2006.
11. Ohno E, Hirooka Y, Kawashima H, et al. Natural history of pancreatic cystic lesions: a multicenter prospective observational study for evaluating the risk of pancreatic cancer. J Gastroenterol Hepatol **33**: 320-328, 2018.
12. Pergolini I, Sahora K, Ferrone CR, et al. Long-term risk of pancreatic malignancy in patients with branch duct intraductal papillary mucinous neoplasm in a referral center. Gastroenterology **153**: 1284-1294, 2017.
13. Tanaka H. Diagnostic opportunities and clinical features of resectable pancreatic cancer: a single center retrospective analysis. Nihon Shokakigankensin Gakkai Zasshi (J Gastrointest Cancer Screen) **60**: 32-40, 2022 (in Japanese, Abstract in English).
14. Mehta HB, Mehta V, Girman CJ, Adhikari D, Johnson ML. Regression coefficient-based scoring system should be used to assign weights to the risk index. J Clin Epidemiol **79**: 22-28, 2016.
15. Kanda Y. Investigation of the freely available easy-to-use software 'EZR' for medical statistics. Bone Marrow Transplant **3**: 452-458, 2013.
16. Tanaka M, Fernández-Del Castillo C, Kamisawa T, et al. Revisions of international consensus Fukuoka guidelines for the management of IPMN of the pancreas. Pancreatology **17**: 738-753, 2017.
17. Kanno A, Masamune A, Hanada K, et al. Multicenter study of

early pancreatic cancer in Japan. Pancreatology **18**: 61-67, 2018.

18. Zanini N, Giordano M, Smerieri E, et al. Estimation of the prevalence of asymptomatic pancreatic cysts in the population of San Marino. Pancreatology **15**: 417-422, 2015.

19. de Oliveira PB, Puchnick A, Szejnfeld J, Goldman SM. Prevalence of incidental pancreatic cysts on 3 tesla magnetic resonance. PLoS One **10**: e0121317, 2015.

20. Soroida Y, Sato M, Hikita H, et al. Pancreatic cysts in general population on ultrasonography: prevalence and development of risk score. J Gastroenterol **51**: 1133-1140, 2016.

21. Ricci C, Migliori M, Imbrogno A, et al. Prevalence of asymptomatic intraductal papillary mucinous neoplasms in healthy and ill populations detected by ultrasonography: a single-center study of 6353 outpatients. Pancreas **48**: 113-120, 2019.

22. Capurso G, Boccia S, Salvia R, et al.; the Italian Association for the Study of the Pancreas (AISP), Intraductal Papillary Mucinous Neoplasm (IPMN) Study Group. Risk factors for intraductal papillary mucinous neoplasm (IPMN) of the pancreas: a multicentre case-control study. Am J Gastroenterol **108**: 1003-1009, 2013.

23. Bartsch DK, Slater EP, Carrato A, et al. Refinement of screening for familial pancreatic cancer. Gut **65**: 1314-1321, 2016.

24. Pergolini I, Schorn S, Jäger C, et al. Diabetes mellitus in intraductal papillary mucinous neoplasms: a systematic review and meta-analysis. Surgery **169**: 411-418, 2021.

25. Matsuda R, Miyasaka Y, Yamada Y, et al. Chronic inflammatory changes and oxidative stress in the background of "pancreatic ductal adenocarcinoma concomitant with intraductal papillary mucinous neoplasm". Virchows Arch **477**: 799-806, 2020.

26. Morales-Oyarvide V, Mino-Kenudson M, Ferrone CR, et al. Diabetes mellitus in intraductal papillary mucinous neoplasm of the pancreas is associated with high-grade dysplasia and invasive carcinoma. Pancreatology **17**: 920-926, 2017.

27. Pergolini I, Jäger C, Safak O, et al. Diabetes and weight loss are associated with malignancies in patients with intraductal papillary mucinous neoplasms. Clin Gastroenterol Hepatol **19**: 171-179, 2021.

28. Carr RA, Roch AM, Shaffer K, et al. Smoking and IPMN malignant progression. Am J Surg **213**: 494-497, 2017.