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Association between severity of pancreatic exocrine insufficiency and computed tomography-based morphological severity in patients with chronic pancreatitis

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Abstract

The association between pancreatic exocrine insufficiency (PEI) and morphologic findings in chronic pancreatitis has not yet been fully studied. Thus, the aim of this study was to investigate the correlation between PEI severity and computed tomography (CT)-based morphological severity in patients with chronic pancreatitis. This nationwide survey included 180 Korean participants with chronic pancreatitis aged 18 years or older between January 2018 and December 2021. PEI severity was measured by the PEI questionnaire (PEI-Q). Morphological severity was measured using a CT-based scoring system, which included pancreatic duct caliber, pancreatic duct stricture or intraductal obstructing calculus, pancreatic atrophy, and pancreatic calcification. In addition, 35 patients who received pancreatic enzyme replacement therapy (PERT) were evaluated by PEI-Q to determine whether PEI improved after PERT. PEI severity was normal (n = 89), mild (n = 69), moderate (n = 14), or severe (n = 8). Severities of pancreatic duct caliber and pancreatic duct stricture or intraductal obstructing calculus had small but significant associations with PEI severity (Cramer V = 0.121 and 0.141, respectively). Severities of pancreatic atrophy and pancreatic calcification were not significantly associated with PEI severity. PEI severity showed a significant improvement after PERT ($P < .001$). In conclusion, PEI severity had significant associations with CT-based morphological severities, including severities of pancreatic duct caliber and pancreatic duct stricture or intraductal obstructing calculus. In addition, PEI-Q could be a useful indicator for evaluating the therapeutic effect of PERT in clinical practice.

Abbreviations: BMI = body mass index, CT = computed tomography, IQR = interquartile range;FE-1 = fecal elastase-1, MRI = magnetic resonance imaging, PEI = pancreatic exocrine insufficiency, PEI-Q = PEI questionnaire, PERT = pancreatic enzyme replacement therapy.

Keywords: chronic pancreatitis, computed tomography, pancreatic exocrine insufficiency

1. Introduction

Pancreatic exocrine insufficiency (PEI) occurs when it cannot maintain normal digestion due to a lack of activity of pancreatic digestive enzymes in the small intestine.[1] Causes of PEI include several pancreatic diseases, cystic fibrosis, celiac disease, and gastrointestinal or pancreatic surgery.[2–5] Among them, chronic pancreatitis is the most common cause of PEI in adults. It can induce morphologic changes such as pancreatic parenchymal atrophy and pancreatic duct dilatation, as well as decreased pancreatic exocrine and endocrine functions.[6] Therefore,

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clinical staging of chronic pancreatitis requires functional tests to evaluate pancreatic exocrine and endocrine functions along with imaging tests of the pancreas.

Among various imaging tests, computed tomography (CT) scan has the advantage of low cost and rapid image acquisition. It is far superior to magnetic resonance imaging (MRI) in detecting pancreatic calcification, which is an important pathological change in chronic pancreatitis.[7] Although the Cambridge classification using endoscopic retrograde cholangiopancreatography, ultrasound, and CT has been reported for evaluating the severity of chronic pancreatitis,[8] it is not widely used in clinical practice. Recently, a CT-based scoring system with a modified Cambridge classification has been reported.[9] It provides more ease in assessing the morphological severity of chronic pancreatitis in clinical practice. Confirmation of the presence or absence of PEI is very important for functional evaluation and treatment of chronic pancreatitis. Although direct functional tests through stimulation of secretin or cholecystokinin are considered the most accurate and reliable standard tests for evaluating exocrine pancreatic function, they are difficult to apply in clinical practice due to technical difficulty and invasive tests. One study has recently reported that the diagnosis and severity of PEI can be evaluated using a PEI questionnaire (PEI-Q), which is easier to access clinically.[10] The diagnosis and severity of PEI have been assessed using the total symptom score, which is the sum of scores of 7 abdominal symptoms and 6 bowel movement symptoms.[10]

If there is an association between PEI, which is a critical functional problem in patients with chronic pancreatitis, and morphological severity, it could be of great clinical help in the initial evaluation and treatment of PEI because the clinical approach of imaging tests is more straightforward. However, existing studies examining the association between PEI and imaging findings in chronic pancreatitis are few in number. In addition, there has been no report about the correlation of severity between PEI and morphologic findings in chronic pancreatitis. Therefore, the aim of this study was to investigate the correlation between the severity of PEI based on PEI-Q and CT-based morphological severity in patients with chronic pancreatitis.

2. Materials and methods

2.1. Study population

This study was a prospective observational study conducted using a nationwide survey of Korean participants aged over 18 years with chronic pancreatitis who visited gastroenterology outpatient clinics at 9 tertiary hospitals in South Korea from January 2018 to December 2021. Patients were excluded if they had cystic fibrosis, acute pancreatitis, pancreatic cancer, a history of gastrointestinal or pancreatic surgery, or if they were unwilling or unable to complete the questionnaire. Additionally, only patients who had undergone CT imaging within 6 months before completing the PEI-Q were included in the study. This study's diagnosis of chronic pancreatitis was based on the revised Cambridge classification. The diagnosis was made by identifying characteristic features of chronic pancreatitis, including pancreatic calcification, ductal irregularity, and parenchymal atrophy, using imaging modalities such as CT, MRI, and endoscopic ultrasound. In addition, the presence of steatorrhea, recurrent abdominal pain, and a history of excessive alcohol consumption or other risk factors were considered in the diagnosis.

2.2. Data collection and definitions of variables

A total of 180 participants consented to participate in this study. The following data were collected for analysis. Demographic and clinical variables included age, gender, body mass index (BMI), drinking and smoking status, etiology of chronic pancreatitis, diabetes mellitus, and history of pancreatic enzyme replacement therapy (PERT).

The severity of PEI (mild, moderate, or severe) was measured using PEI-Q by calculating a total symptom score. The severity of PEI was defined according to a previous study as follows: a total symptom score of greater than or equal to 0.60, a diagnosis of PEI; a total symptom score of greater than or equal to 1.8, severe PEI; a total symptom score of greater than or equal to 1.4 to 1.8, moderate PEI; and a total symptom score of greater than or equal to 0.60 to 1.4, mild PEI.[10]

Morphological severity of chronic pancreatitis was measured using a CT-based scoring system, according to a previous study.[9] CT scan images were reviewed by a subspecialty-trained abdominal radiologist with over 10 years of experience, who was blinded to clinical information. Images were analyzed for the presence and severity of parenchymal and ductal changes (Figure S1, Supplemental Digital Content, http://links.lww.com/MD/O75). The severity of pancreatic duct caliber was defined as follows: <3.5 mm, mild; 3.5 to 7 mm, moderate; and >7 mm, severe. The severity of pancreatic duct stricture or intraductal obstructing calculus was defined according to the location of the lesion (tail, mild; body, moderate; and head, severe). The severity of pancreatic atrophy was defined according to the thickness of the pancreas measured at the level of the left border of the adjacent vertebral body on the axial view of CT as follows: >14 mm, mild; 7 mm to 14 mm, moderate; and <7 mm, severe. The severity of pancreatic calcification was defined according to the number of calcifications as follows: punctate calcification, <3 mm in size; coarse calcification, greater than or equal to 3 mm in size; less than 7 punctate calcifications, mild; 7 to 50 punctate calcifications or less than 7 coarse calcifications, moderate; and greater than or equal to 7 coarse calcifications, severe. The morphological severity was graded based on a combination of features, including main pancreatic ductal dilatation and contour irregularity, pancreatic calcifications, and pancreatic parenchymal atrophy (Table S1, Supplemental Digital Content, http://links.lww.com/MD/O75).[9]

Participants who underwent PERT received pancreatin (Creon® 25,000; Abbott, Hannover, Germany or Norzyme® 25,000; Nordmark Arzneimittel GmbH & Co., Uetersen, Germany). They were instructed to consume a total of 6 to 9 capsules per day orally (2 capsules with each main meal, 3 meals per day; and 1 capsule with each snack, up to 3 snacks per day). PEI severity was assessed with PEI-Q before PERT and 1 month after PERT.

2.3. Ethics statement

The study protocol was approved by the institutional review boards of all the participating hospitals (Gyeongsang National University Changwon Hospital [No. 2021-05-034], Seoul National University Hospital [No. H-2106-093-1228], Seoul St. Mary Hospital [No. KC20OISI0022], Pusan National University Hospital [No. 2208-030-118], Yonsei University College of Medicine [No. 4-2021-1257], Korea University Ansan Hospital [No. 2020AS0337], Gil Medical Center [No. 2014-162], Seoul National University Boramae Medical Center [No. DUIH 2021-10-016], and Kyungpook National University Hospital [No. KNUH 2021-05-040]). Informed consent was obtained from all patients.

2.4. Statistical analysis

Patient characteristics were described as number (%) for categorical variables and median (interquartile range [IQR]) for continuous variables. In univariate analyses, analysis of variance (ANOVA) and Chi-square test or Fisher exact test were used for comparison of continuous or categorical variables, respectively.

The Cochran-Armitage trend test was used to evaluate the association between the prevalence of PEI and CT-based morphological severity. The Cramer V was used to identify the association between PEI severity and CT-based morphological severity. The strength of the association was determined based on the value of Cramer V as follows: <0.06, no association; 0.06 to <0.17, small association; 0.17 to <0.29, medium association; and more than 0.29, large association. The McNemar test was used to compare PEI severity changes before and after PERT. All analyses were performed using statistical software R version 4.1.2 (Development Core Team. R Foundation for Statistical Computing, Vienna, Austria). *P* values < .05 were considered statistically significant.

3. Results

3.1. Clinical characteristics of the study population according to PEI severity based on PEI-Q

Demographic and clinical characteristics of all 180 patients with chronic pancreatitis according to PEI severity are summarized in Table 1. PEI severity was normal (n = 89), mild (n = 69), moderate (n = 14), or severe (n = 8). Patients without PEI (median age: 64 years, IQR: 57–71 years) were significantly older than patients with PEI (median age: 60 years, IQR: 50.5–66.5 years). BMI was significantly lower with increasing severity of PEI (*P* = .007). There was no significant difference in gender, drinking or smoking status, etiology of chronic pancreatitis, diabetes mellitus, or history of PERT between the 2 groups.

3.2. Prevalence of PEI according to CT-based morphological severity in patients with chronic pancreatitis

The prevalence of PEI was significantly higher in patients with severe pancreatic calcification than in those with normal, mild, or moderate pancreatic calcification (Chi-square test *P* = .041, Cochran–Armitage trend test *P* = .005). There was no significant difference in the prevalence of PEI according to other CT-based morphological severities, including pancreatic duct caliber, pancreatic duct stricture or intraductal obstructing calculus, or pancreatic atrophy. The prevalence of PEI was lower (34.4%) in patients with normal chronic pancreatitis than in those with more severe chronic pancreatitis (36.8–60.3%) in grading of morphological severity, although the difference was not statistically significant (Chi-square test *P* = .052) (Table 2).

3.3. Association between PEI severity based on PEI-Q and CT-based morphological severity in patients with chronic pancreatitis

Table 3 presents associations of PEI severity with each CT-based morphological severity. Severities of pancreatic duct caliber and pancreatic duct stricture or intraductal obstructing calculus had small but significant associations with PEI severity (Cramer V = 0.121 and 0.141, respectively). The severity of pancreatic atrophy was not significantly associated with PEI severity (*P* = .45, Cramer V = 0). Severities of pancreatic calcification and grading of morphological severity had small associations with PEI severity, although they were not statistically significant (*P* = .11 and *P* = .16, respectively).

3.4. Changes of PEI severity evaluated by PEI-Q after PERT in patients with chronic pancreatitis

A total of 35 patients underwent PERT. Their changes in PEI severity after PERT were assessed using PEI-Q. The severity of PEI before PERT was mild (n = 24), moderate (n = 6), or severe (n = 5). The severity of PEI after PERT was normal (n = 16), mild (n = 16), moderate (n = 2), or severe (n = 1). After PERT, the severity of PEI was improved in 22 (62.9%) patients. The

Table 1

Baseline characteristics of study population according to pancreatic exocrine insufficiency severity based on pancreatic exocrine insufficiency questionnaire.

	PEI severity				
	Normal	Mild	Moderate	Severe	
Variables	n = 89	n = 69	n = 14	n = 8	*P* value
Age (years)*	64 (57–71)	62 (53–69)	54.5 (47–60)	55 (49.5–61)	.005
Gender					.364
Male	70 (78.7)	56 (81.2)	13 (92.9)	5 (62.5)	
Female	19 (21.3)	13 (18.8)	1 (7.1)	3 (37.5)	
BMI (kg/m^2)	22.7 (20.8–24.5)	21.6 (19.7–24)	20.4 (17.1–22.5)	19.5 (19–21.9)	.007
Alcohol					.171
Nondrinker	23 (25.9)	17 (24.7)	1 (7.2)	1 (12.5)	
Ex-drinker	48 (53.9)	31 (44.9)	8 (57.1)	7 (87.5)	
Current drinker	18 (20.2)	21 (30.4)	5 (35.7)	0 (0)	
Smoking					.189
Nonsmoker	30 (33.7)	25 (36.2)	2 (14.3)	2 (25)	
Ex-smoker	31 (34.8)	19 (27.6)	2 (14.3)	2 (25)	
Current smoker	28 (31.5)	25 (36.2)	10 (71.4)	4 (50)	
Etiology					.593
Alcohol	51 (57.3)	45 (65.2)	9 (64.3)	7 (87.5)	
Idiopathic	29 (32.6)	21 (30.4)	5 (35.7)	1 (12.5)	
Others†	9 (10.1)	3 (4.4)	0 (0)	0 (0)	
Diabetes mellitus	36 (40.4)	34 (49.3)	10 (71.4)	4 (50)	.163
History of PERT	30 (33.7)	32 (46.4)	9 (64.3)	5 (62.5)	.062

Other values are presented as number (%).

BMI = body mass index, PEI = pancreatic exocrine insufficiency, PERT = pancreatic enzyme replacement therapy.

* Values are presented as median (interquartile range).

† Other etiologies included gallstone (n = 5), hypertriglyceridemia (n = 4), trauma (n = 2), or pancreas divisum (n = 1).

remaining 13 (37.1%) patients had no change. As a result, PEI severity showed a significant improvement after PERT ($P < .001$) (Fig. 1).

Table 2

Prevalence of pancreatic exocrine insufficiency according to computed tomography-based morphological severity in patients with chronic pancreatitis.

CT-based morphological severity		Prevalence of PEI	*P* value
PD caliber	Normal	46.4% (26/56)	.053*
	Mild	34.2% (13/38)	.078**
	Moderate	64.9% (24/37)	
	Severe	57.1% (28/49)	
PD stricture/intraductal obstructing calculus	Normal	47.9% (45/94)	.129*
	Mild	20.0% (2/10)	.166**
	Moderate	56.2% (9/16)	
	Severe	58.3% (35/60)	
Pancreatic atrophy	Normal	41.9% (18/43)	.178*
	Mild	45.5% (30/66)	.05**
	Moderate	62.2% (23/37)	
	Severe	58.8% (20/34)	
Pancreatic calcification	Normal	38.1% (16/42)	.041*
	Mild	42.5% (17/40)	.005**
	Moderate	52.2% (24/46)	
	Severe	65.4% (34/52)	
Grading of morphological severity	Normal	34.4% (11/32)	.052*
	Mild	51.0% (26/51)	.025**
	Moderate	36.8% (7/19)	
	Severe	60.3% (47/78)	

CT = computed tomography, PD = pancreatic duct, PEI = pancreatic exocrine insufficiency.

* Chi-square test with Fisher exact test.

** Cochran–Armitage trend test.

4. Discussion

PEI is one of the common complications in patients with chronic pancreatitis. It increases the risk of nutritional deficiencies, particularly fat, protein, and fat-soluble vitamins.[11,12] It might increase mortality due to malnutrition.[13] Therefore, it is very important to properly evaluate and treat PEI in patients with chronic pancreatitis. Clinical staging of chronic pancreatitis requires imaging and functional tests of the pancreas. Among them, imaging tests for morphologic evaluation have the advantage of easier clinical application than pancreatic exocrine tests. However, studies on the association between PEI and morphologic findings in chronic pancreatitis are still lacking. The current study showed that severities of pancreatic duct caliber and pancreatic duct stricture or intraductal obstructing calculus were significantly associated with PEI severity in patients with chronic pancreatitis. The prevalence of PEI was significantly increased according to the severity of pancreatic calcification. In addition, the severity of PEI had a significant improvement after PERT in chronic pancreatitis with PEI.

CT is the most common imaging modality used in clinical practice. It has a high accuracy in detecting pancreatic parenchymal and ductal features of chronic pancreatitis. Thus, the current study chose CT. Chronic pancreatitis has various morphologic findings on CT, ranging from normal to severe changes, including marked pancreatic ductal dilation or irregular stricture, pancreatic atrophy, and calcifications. However, the lack of previous studies on the association between morphologic and functional findings in chronic pancreatitis makes it difficult for clinicians to accurately assess the current stage of the disease and PEI. A recent retrospective study has reviewed CT and/or MRI in patients with idiopathic chronic pancreatitis.[14] It found that patients with low fecal elastase-1 (FE-1) had a significantly wider pancreatic duct caliber with a

Table 3

Correlation between pancreatic exocrine insufficiency severity based on pancreatic exocrine insufficiency questionnaire and computed tomography-based morphological severity in patients with chronic pancreatitis.

	PEI severity						
CT-based morphological severity	Normal n = 89	Mild n = 69	Moderate n = 14	Severe n = 8	Total n = 180	*P* value	Cramer V
PD caliber						.028	0.121
Normal	30 (53.6)	22 (39.3)	3 (5.4)	1 (1.8)	56 (100)		
Mild	25 (65.8)	6 (15.8)	3 (7.9)	4 (10.5)	38 (100)		
Moderate	13 (35.1)	18 (48.6)	4 (10.8)	2 (5.4)	37 (100)		
Severe	21 (42.9)	23 (46.9)	4 (8.2)	1 (2)	49 (100)		
PD stricture/intraductal obstructing calculus						.022	0.141
Normal	49 (52.1)	37 (39.4)	6 (6.4)	2 (2.1)	94 (100)		
Mild	8 (80)	1 (10)	1 (10)	0 (0)	10 (100)		
Moderate	7 (43.8)	3 (18.8)	3 (18.8)	3 (18.8)	16 (100)		
Severe	25 (41.7)	28 (46.7)	4 (6.7)	3 (5)	60 (100)		
Pancreatic atrophy						.45	0
Normal	25 (58.1)	15 (34.9)	2 (4.7)	1 (2.3)	43 (100)		
Mild	36 (54.6)	21 (31.8)	6 (9.1)	3 (4.6)	66 (100)		
Moderate	14 (37.9)	16 (43.2)	5 (13.5)	2 (5.4)	37 (100)		
Severe	14 (41.2)	17 (50)	1 (2.9)	3 (5.9)	34 (100)		
Pancreatic calcification						.11	0.105
Normal	26 (61.9)	14 (33.3)	1 (2.4)	1 (2.4)	42 (100)		
Mild	23 (57.5)	15 (37.5)	1 (2.5)	1 (2.5)	40 (100)		
Moderate	22 (47.8)	17 (37)	6 (13)	1 (2.2)	46 (100)		
Severe	18 (34.6)	23 (44.2)	6 (11.5)	5 (9.6)	52 (100)		
Grade of morphological severity						.16	0.088
Normal	21 (65.6)	11 (34.4)	0 (0)	0 (0)	32 (100)		
Mild	25 (49)	19 (37.2)	6 (11.8)	1 (2)	51 (100)		
Moderate	12 (63.1)	5 (26.3)	1 (5.3)	1 (5.3)	19 (100)		
Severe	31 (39.7)	34 (43.6)	7 (9)	6 (7.7)	78 (100)		

All values are presented as number (%).

PD = pancreatic duct, PEI = pancreatic exocrine insufficiency.

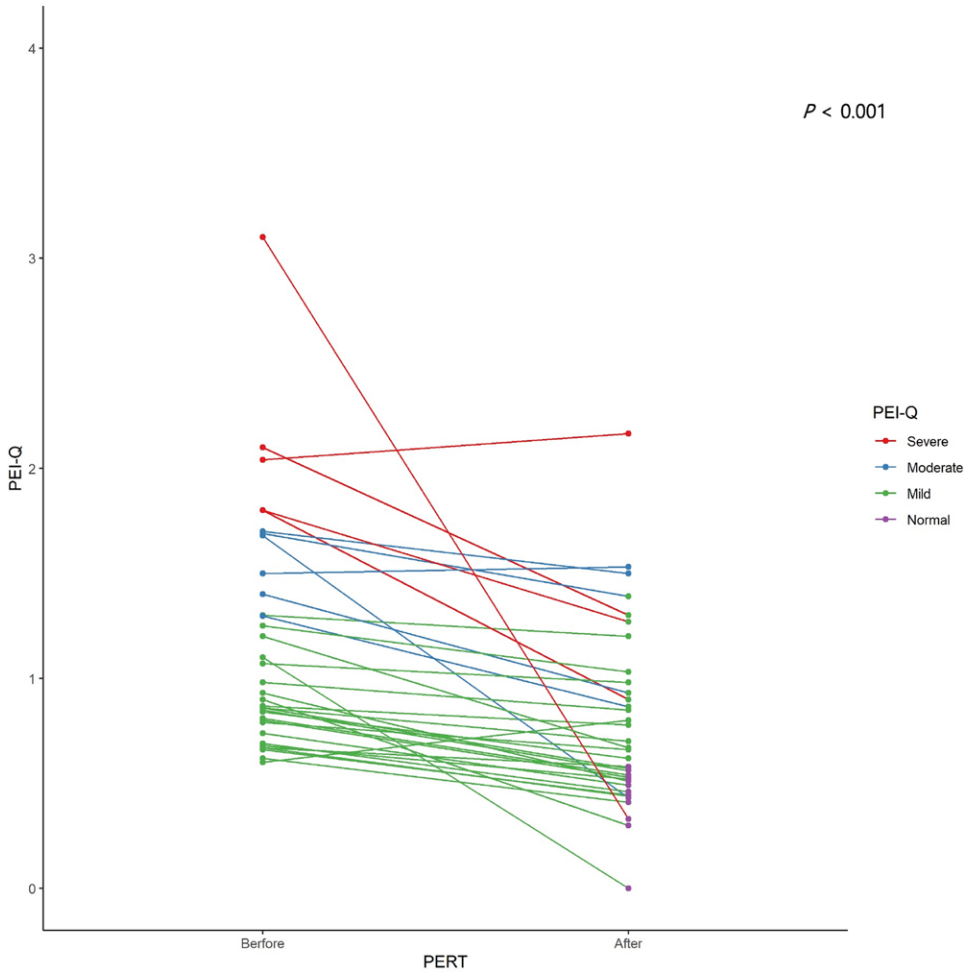

Figure 1. Changes of pancreatic exocrine insufficiency severity based on pancreatic exocrine insufficiency questionnaire after pancreatic enzyme replacement therapy in chronic pancreatitis with pancreatic exocrine insufficiency (n = 35). PEI-Q = pancreatic exocrine insufficiency questionnaire; PERT = pancreatic enzyme replacement therapy.

mean of 8.2 ± 4.2 mm compared with 4.2 ± 1.7 mm for those with normal FE-1 ($P < .001$).[14] In addition, there was a significant association between low FE-1 and the presence of intraductal calculus in the head and neck region of the pancreas ($P < .001$).[14] Similar to these findings, our study showed that severities of pancreatic duct caliber and pancreatic duct stricture or intraductal obstructing calculus were significantly associated with PEI severity. Although there is a limitation of direct comparison with the current study because of different imaging tools, a previous prospective study on endoscopic ultrasonography findings has reported that the presence of dilated main pancreatic duct and intraductal calculus is significantly associated with PEI in chronic pancreatitis,[15] consistent with our findings. However, the association between PEI and CT-based morphological findings in chronic pancreatitis remains unclear as only 3 studies have reported correlations of PEI with CT findings, including the current study. Therefore, a further large prospective study is necessary to verify our findings.

A previous study has reported that the prevalence of PEI is not statistically different according to grading of morphological severity based on CT in patients with chronic pancreatitis,[9] consistent with our study. In addition, the current study showed no significant association between PEI severity and grading of morphological severity in chronic pancreatitis. In a previous study, the prevalence of PEI was more frequent in patients with severe pancreatic atrophy than in those who had no pancreatic atrophy or mild or moderate pancreatic atrophy ($P = .01$).[9] However, our study showed that the severity of pancreatic atrophy was not significantly associated with the prevalence or severity of PEI. Due to the lack of existing studies regarding the association between PEI and CT findings in chronic pancreatitis, it is difficult to accurately explain this difference. However, a previous study on endoscopic retrograde cholangiopancreatography or CT findings has reported that the development of PEI in patients with chronic pancreatitis depends primarily on the degree of ductal changes, while parenchymal abnormalities play a less important role.[16] Similarly, we found that the severity of pancreatic ductal abnormalities, including dilation, stricture, and intraductal calculus, had a more significant association with PEI severity than the severity of pancreatic parenchymal abnormalities, including atrophy and calcification. However, a further large prospective study is needed to verify this finding.

The current study used PEI-Q to assess the diagnosis and severity of PEI in chronic pancreatitis. A previous study has reported that PEI-Q has good validity and reliability in evaluating PEI in patients with chronic pancreatitis.[10] Although PEI-Q has been validated to a limited extent in the UK, Germany, France, and Spain in a previous study, recruited patients had diverse demographic characteristics.[10] Thus, findings are likely to represent the PEI experience of patients with chronic pancreatitis across a range of countries.[10] In addition, a Dutch population-based cohort study has reported that patients with chronic pancreatitis and PEI have lower BMI.[17] Nutritional deficiencies may worsen according to increasing PEI severity,

which may lead to more severe weight loss and may be associated with a decrease in BMI. The current study showed that BMI was significantly lower with increasing severity of PEI in baseline characteristics. Therefore, the severity of PEI assessed by PEI-Q in our study might be indirectly appropriate. However, further validation studies on PEI-Q in Korea are needed in the future.

In previous prospective multicenter observational studies, PERT significantly improved PEI-related symptoms and quality of life in chronic pancreatitis with PEI,[18,19] consistent with our finding based on PEI-Q. Therefore, PERT is recommended for symptomatic or diagnosed patients with PEI in chronic pancreatitis. PEI-Q is expected to be a useful indicator for evaluating the therapeutic effect of PERT in clinical practice.

Our study has some limitations. First, the evaluation for PEI severity was obtained from self-reported questionnaires (PEI-Q) during outpatient care. Therefore, we cannot rule out the possibility of response bias caused by respondents failing to provide correct information. Second, we could not compare the PEI-Q results with traditional pancreatic exocrine function tests, which could have further validated our findings. Third, among patients with PEI, the numbers of patients with moderate PEI (n = 14, 7.8%) and severe PEI (n = 8, 4.4%) were relatively small. Therefore, a further prospective multicenter randomized study including sufficient patients with PEI of various severity and pancreatic exocrine tests such as FE-1 is needed to confirm the current observations. Nevertheless, to the best of our knowledge, our work is the first study identifying the association between PEI severity and CT-based morphological severity in patients with chronic pancreatitis.

In conclusion, our results demonstrated a significant association between PEI severity and CT-based morphological severity, including pancreatic duct caliber and pancreatic duct stricture, or intraductal obstructing calculus, in chronic pancreatitis. In addition, PERT significantly improved the severity of PEI. It was found that PEI-Q could be a useful indicator to assess whether PEI has improved after PERT. These findings might help other clinicians struggling with evaluating and treating PEI in patients with chronic pancreatitis. However, further studies are necessary to confirm the association between PEI severity and CT-based morphological severity in chronic pancreatitis.

Author contributions

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