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Background / Aim: This study investigates the prevalence and consequences of mutations in the CFTR, PRSS1, and SPINK1 genes in idiopathic pancreatitis patients, aiming to compare the genetic, clinical, and morphological characteristics, as well as the long-term outcomes between patients with gene-associated chronic pancreatitis (GCP) and those with alcoholic chronic pancreatitis (ACP).

Method: From January 1997 to July 2023, a total of 670 patients with idiopathic pancreatitis were prospectively enrolled and subjected to DNA testing for comprehensive genetic profiling of CFTR, SPINK1, and PRSS1 genes and their variants. A propensity score-matched study was conducted, including patients with GCP and matched on a 1:3 ratio to patients with ACP based on nearest neighbor propensity scores calculated using three variables: age, gender, BMI, and smoking history.

Result: Gene mutations were identified in 24.3% of patients with idiopathic pancreatitis. The most frequently identified SPINK1 variant was the IVS3+2T>C heterozygote (13.9%). Pancreas divisum was more commonly associated with CFTR mutations (47.1%) compared to other mutations (SPINK1, 15.3%; PRSS1, 7.1%) (p=0.005). Patients in the GCP group had a significantly younger median age at symptom onset (26.2 years vs. 40.7 years, $p < 0.0001$) and new onset of DM (56.1 years vs. 64.8 years, $p < 0.0001$) compared to those in the ACP group. Pancreatic cancer incidence was higher in the GCP group (3.2%) compared to the ACP group (0.6%), with a statistically significant difference ($p = 0.027$). Univariate and multivariate logistic regression analyses revealed that patients with gene mutation-associated chronic pancreatitis had significantly higher odds of developing pancreatic cancer compared to those with alcoholic chronic pancreatitis (univariate OR: 5.125, 95% CI: 1.24-25.21, $p = 0.026$; multivariate OR: 6.04, 95% CI: 1.42-30.46, $p = 0.017$).

Conclusions: In a comprehensive analysis of CFTR, PRSS1, and SPINK1 gene mutations in idiopathic pancreatitis, the SPINK1 mutation emerged as the most prevalent. Pancreas divisum was frequently associated with CFTR mutations.

GCP is characterized by an earlier onset of symptoms, pancreatic insufficiencies, and an elevated risk of pancreatic cancer, emphasizing the need for genetic testing in the diagnosis and management of pancreatitis

Risk factor of pancreatic cancer

	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	Adjusted OR	95% CI	P value
Age	1.063	1.01-1.12	0.017			
Smoking	0.445	0.09-1.83	0.271			
Obesity	0.841	0.25-2.80	0.776			
DM	3.273	0.80-16.07	0.106			
Gene mutation	5.125	1.24-25.21	0.026	6.04	1.42-30.46	0.017
IVS3+2T>C mutation	5.863	1.36-25.18	0.013	7.82	1.72-35.77	0.006

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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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Background: The association between pancreatic exocrine insufficiency (PEI) and morphologic findings in chronic pancreatitis has not been fully studied yet. 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.

Methods: This nation-wide survey included 180 Korean participants with chronic pancreatitis aged 18 years or older between January 2018 and December 2021. PEI severity was measured by PEI questionnaire (PEI-Q). Morphological severity was measured using a CT-based scoring system including 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.

Results: 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's $V = 0.121$ 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 ($P < 0.001$).

Conclusions: 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 therapeutic effect of PERT in clinical practice.

Chaired poster
CP
Pancreatic Cancer – Basic Science
Thursday, June 27th, 14:15 - 15:00

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Transcriptomic molecular subtypes stratify duodenum ampulla of Vater carcinoma

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Objective: Duodenum ampulla of Vater carcinoma (DAC) represents a molecularly diverse disease characterized by varied clinical outcomes. The complexity and lack of clarify in their histopathological and molecular subtypes hinder their clinical management.

Design: This study employed single-cell and bulk transcriptome sequencing to achieve molecular classification of DAC. We performed an unsupervised clustering on a retrospective cohort consisting of 113 DAC patients and characterized the molecular features and tumor microenvironment.

Results: Single-cell transcriptomic profiling revealed heterogeneous gene expression patterns in epithelial cells within DAC tumors. Focusing on the highly variable genes identified by single-cell transcriptomes of tumor epithelial cells, we developed an ampullar carcinoma molecular stratification (AMS) model to upgrade histopathological subtyping. This binary AMS subtypes included classical and mesenchymal DAC, which were based on the expression profiling of tumor tissues. Clinical correlation analysis confirmed that the AMS classification is an independent predictor of postoperative survival in patients with DAC, and pathological correlation analysis revealed that desmoplastic stroma in the mesenchymal subtype was associated with poor prognosis. Moreover, HSPB6