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Comprehensive Assessment of Direct and Passive Smoking Across the Pancreatitis Spectrum

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Abstract

Objectives: Smoking is a key risk factor for pancreatitis, contributing to pathogenesis and disease progression. Data regarding secondhand smoking, or passive smoking (PS) exposure, are lacking. We therefore aimed to assess the impact of PS exposure across the pancreatitis spectrum.

Methods: We analyzed baseline data from the PROCEED study, a multicenter study in the US including patients with acute (AP), recurrent acute (RAP), and chronic (CP) pancreatitis. Participants detailed their individual smoking history and PS exposure, which was compared between AP, RAP, and CP subgroups. Participant factors and clinical characteristics were compared by level of individual and PS exposure.

Results: Among 1369 participants (190 AP, 498 RAP, 681 CP), 346 (25.3%) were current and 409 (29.9%) were former smokers. The CP subgroup had the highest proportion of current smokers (36.7% CP vs. 15.1% RAP, 11.1% AP, $p<0.001$). PS exposure was also significantly higher in the CP subgroup (68.6% CP vs. 58.2% RAP, 55.3% AP, $p<0.001$). A minority (16.3%) with CP reported no smoking exposure (by self or passive) while nearly half smoked ≥ 20 pack-years. The mean PS duration was significantly higher in CP participants (21.8 years) compared to those with AP (17.8 years) or RAP (18.9 years) ($p<0.0166$).

Conclusions: In this multicenter study, we affirmed an association with smoking use and intensity with CP-related complications. For the first time we report a high prevalence of prior exposure to passive smoking in all pancreatitis subtypes, which require further study to understand the impact on disease outcomes.

Keywords: chronic pancreatitis; passive smoking; secondhand smoking; smoking; acute pancreatitis; acute recurrent pancreatitis

INTRODUCTION

Cigarette smoking represents a known independent risk factor for the development of chronic pancreatitis (CP).[1-4] Not only does smoking increase the risk of developing CP after an initial episode or recurrent episodes of acute pancreatitis (AP), but smoking also accelerates disease progression within CP with several studies reporting earlier onset of calcifications as well as exocrine and endocrine insufficiency.[5-7] In addition to playing a harmful role in the pathogenesis and progression of CP, smoking has also been associated with pain and poor quality of life in patients with CP.[8, 9] The mechanism of the deleterious effects of smoking on the pancreas are likely multifactorial; ranging from inducing pancreatic ductal dysfunction to activating the inflammatory cascade and causing oxidative stress in the pancreas.[3]

Despite the numerous studies implicating personal smoking history as a risk factor for CP, few studies have examined the effects of second-hand smoking, or passive smoking exposure, on the development and progression of CP.[10] The negative effects of passive smoking are well-known, ranging from increased risk in malignancies such as lung cancer to increased risk of chronic conditions such as coronary artery disease and chronic obstructive pulmonary disease.[11-14] Nevertheless, given that smoking itself is an underappreciated risk factor for CP, the potential impact of passive smoking exposure remains even less understood.[15]

The Prospective Evaluation of Chronic Pancreatitis for Epidemiologic and Translational Studies (PROCEED) is a prospective, multicenter cohort study (ClinicalTrials.gov NCT3099850) in the United States. PROCEED has been longitudinally following participants with pancreatic diseases ranging from AP to recurrent acute pancreatitis (RAP) to CP.[16] Detailed

data regarding smoking and other etiologic risk factors are prospectively assessed, which makes this an excellent study population to evaluate direct and passive smoking exposure across the pancreatitis spectrum. Therefore the aim of this study was to detail the level of direct and passive smoking exposure in the pancreatitis population.

METHODS

This cross-sectional analysis utilized data collected at enrollment from adult participants in the PROCEED study, conducted through the Consortium for the Study of Chronic Pancreatitis, Diabetes, and Pancreatic Cancer (CPDPC) that includes 10 clinical centers and a data coordinating center.[16] Each of the study sites involved in the PROCEED study received institutional review board approval. All authors had access to the data and reviewed and approved this manuscript.

Study setting and definitions

Data from participants who enrolled between June 2017 to June 2024 was included. For the purpose of this study, we included participants with a single documented episode of AP within 18 months prior to enrollment, those with two or more documented episodes of pancreatitis (RAP) and those with definite CP. Of note, the PROCEED study excluded participants with AP with etiology secondary to gallstones, medications, trauma or autoimmune pancreatitis.[16] Definite CP was defined as the presence of pancreatic calcifications or Cambridge classification of 3 or 4 on either computed tomography (CT) or magnetic resonance cholangiopancreatography (MRCP).[16, 17] As the primary purpose of PROCEED is to recapitulate the natural history of CP, participants were enrolled with purposeful representation from AP, RAP and CP populations to enable

observation of disease progression and test predictive biomarkers for incident CP in the AP/RAP participants and new-onset diabetes in CP participants. Healthy participants (American Society of Anesthesiologists Class I and II) without pancreatic diseases were also enrolled to serve as a control population for biomarker testing.[18] The study is under active recruitment.

Case report forms were completed by study participants as well as study coordinators and site investigators at the time of enrollment. As described previously, collected data included detailed participant demographic data and socioeconomic data as well as disease-related data.[16] Participants also completed a questionnaire measuring patient-reported outcomes such as quality of life and pain. Pain was additionally assessed through this case report form, specifically addressing the severity of pain as well as temporality of pain in the year prior to enrollment.

Smoking Assessment

Tobacco use was assessed at enrollment to measure each participant's direct exposure and passive exposure to various forms of tobacco. With regard to cigarette (combustible) smoking exposure, participants reported their current use of cigarettes, any prior use of cigarettes, including age of onset, duration, intensity and frequency of cigarette use, and age of quitting, as applicable. In terms of passive smoking exposure, participants reported if they had ever lived with anyone who smoked (cigarettes) regularly, their duration of living with a smoker, and the number of co-residing individuals who smoked.

Covariates

Demographic variables included age, sex, race, ethnicity and body mass index. Socioeconomic factors were self-reported including level of education, income level, employment status and marital standing. Disease-related characteristics were reviewed by study physicians including

etiology, medication use, presence of diabetes (defined using blood glucose level or hemoglobin A1c level in accordance to the American Diabetes Association criteria), exocrine pancreatic dysfunction (EPD), and disease duration (first episode of AP or diagnosis to time of enrollment). Additional CP-related variables included presence of calcifications, level of parenchymal atrophy on imaging, and presence of pancreatic duct strictures and/or stones on imaging.

Statistical Analysis

Summary statistics were compared between the 3 pancreatitis subgroups (AP, RAP, and definite CP). Missing data were excluded from these descriptive statistics. Cross-tabulation was performed to stratify the pancreatitis subgroups by smoking status (never-smoker, former smoker, current smoker), and passive smoking status (lived with a smoker for at least 1 year). Among those exposed to passive smoking, we grouped participants' own smoking intensity (never-smoker , <20 pack-years, ≥ 20 pack-years). Continuous variables were compared across groups using the Kruskal-Wallis test. For categorical variables, comparisons were made using the Chi-Square test, with Fisher's exact test applied when at least one cell frequency was less than 5. The proportional odds model was used to compare ordinal variables. All statistical analyses were performed using a combination of SAS version 9.4 (SAS Institute Inc., Cary, North Carolina, USA) and R version 3.4. A p-value < 0.05 was considered statistically significant for all comparisons.

RESULTS

Study Population

A total of 1369 participants were included in this study, with CP representing the largest subgroup (n=681), followed by RAP (n=498), and AP (n=190). The sample sizes reflect available data as of August 2024 on participants enrolled into the PROCEED study. The median age was higher in the CP subgroup while sex distribution was similar between groups (**Table 1**). Within the overall study population, 346 (25.3%) were current smokers and 409 (29.9%) participants reported smoking in the past. Less than half of participants (n=580, 42.4%) reported being a never-smoker.

Smoking Intensity

The proportion of current smokers was highest in the CP subgroup (36.7%), followed by the RAP subgroup (15.1%) and lastly the AP subgroup (11.1%). Among current smokers, 56% of those with CP reported a ≥ 20 pack-year history, 28% of those with RAP reported a ≥ 20 pack-year history, and 38.1% of those with AP reported a ≥ 20 pack-year history (**Table 1**).

Categorizing lifetime smoking exposure as ≥ 20 pack-years vs < 20 pack-years across the spectrum of smoking, participants with CP had the greatest proportion of those with a ≥ 20 pack-year history (CP 33.0% vs. 10.5% AP vs. 11.9% RAP, $p<0.01$). Comparisons of lifetime smoking exposure between the different pancreatitis subgroups are displayed in **Figure 1**.

Passive Smoking

Overall, passive smoking exposure by way of living with a smoking household member was reported by 62.9% (861/1369) of participants with any stage of pancreatitis. The median duration of passive smoking exposure was 18 years for both never-smokers (IQR 11, 20) and former smokers (IQR 10, 25) and 20 years (IQR 12, 35) in current smokers. Among never-smokers, nearly half of all participants had a history of passive smoking exposure (47.1%, 273/580).

Conversely, the majority of current smokers (84.1%, 291/346) and former smokers (72.9%, 298/409) reported passive smoking exposure.

Distributions of passive smoking by disease and personal smoking status are presented in **Table 2** and **Figure 2**. Comparing passive smoking between the different cohorts, a greater proportion of participants with CP had passive smoking exposure compared to the AP and RAP cohorts (68.7% CP vs. 55.5% AP vs. 57.8% RAP). Participants with CP also had a longer exposure duration compared to those with AP or RAP [median (IQR) values of 18 years (11.5, 30) for CP, 18 years (10, 21) for AP, and 18 years (11, 22) for RAP ($p = 0.017$)]. Additionally, participants with CP were more likely to be exposed to multiple smokers with 4.16% reporting exposure to more than two smoking individuals, compared to 0.51% in AP and 3.29% in RAP ($p < 0.001$). Across all patient categories, passive smoking exposure was most common in current smokers, followed by former smokers than among never smokers.

Among never-smokers, passive smoking exposure was reported in 48.6% of participants with CP, 46.2% of participants with RAP, and 45.9% of participants with AP. For reference, in our control cohort (n=255), 38.4% of never-smokers reported a history of passive smoking exposure. There was only a small portion of CP participants (16.3%, n=111) who had neither personal history nor passive exposure to smoking; this proportion was similarly small in AP and RAP subgroups (data not shown).

Association of Smoking with Sociodemographic and Clinical Characteristics

Within the CP cohort, current smokers had the lowest level of education with 14.4% having a college degree or higher as compared to former (29.6%) or never smokers (45.6%) (**Table,**

Supplemental Digital Content 1, http://links.lww.com/MPA/B470). This trend was similarly seen in the RAP cohort. Current smokers reported a significantly lower level of income than former smokers and non-smokers, which was most pronounced in the CP cohort, where 58% of current smokers had an income < $50,000 as compared to 32.5% of former and 33.5% of never smokers. Relatedly, 50.4% of current smokers with CP were unemployed as compared to former (22.7%) or never (26.1%) smokers with CP.

Within those with CP, the highest proportion of those with severe pain was found in current smokers (65.6%) compared to 50.7% in never-smokers. A higher proportion of current smokers (48%) were also found to have constant pain as compared to never smokers (24%) (**Table 3**).

In participants with CP, calcifications were seen more frequently on imaging in current smokers (82%) and former smokers (75.9%) compared to never-smokers (66.5%). Pancreatic duct strictures were also more frequently found in current smokers (53.2%) and former smokers (49.3%) compared to never-smokers (41.7%). Pancreatic duct stones were most commonly found in current smokers (53.6%) compared to former smokers (37.9%) and never-smokers (35.2%). Lastly, current smokers with CP had the most amount of atrophy on imaging (54.4%) in relation to former smokers (47.3%) and never-smokers (50.4%).

In never-smokers with CP (n=105), there was no difference in pain severity or temporality between those with no passive smoking exposure, those with <20 years of passive smoking exposure and those with ≥20 years of passive smoking exposure (**Table 4**). The proportion of never-smokers with pancreatic exocrine dysfunction, however, significantly increased with level of passive smoking exposure (**Table, Supplemental Digital Content 2, http://links.lww.com/MPA/B471**).

In comparing clinical outcomes between those with and without passive smoking exposure among never-smokers with pancreatitis, no significant differences were found (**Table, Supplemental Digital Content 3, http://links.lww.com/MPA/B472**).

DISCUSSION

This study provides clarity into the exposure level of patients with pancreatitis to cigarette smoking, both personal and passive, demonstrating that both personal history of smoking and passive exposure are common in the pancreatitis population. More than half of patients with pancreatitis reported a history of smoking and nearly half of all patients had a history of passive smoking exposure as well. This was most pronounced in CP, where approximately 15% had absence of personal and passive smoking exposure. We redemonstrated that smoking was associated with advanced disease features of CP, including pancreatic calcifications, pancreatic duct strictures and stones, and atrophy. Moreover, severe pain and constant pain were reported more frequently in current smokers compared to non-smokers and former smokers, further demonstrating the debilitating association of smoking with CP.

There has been a paucity of studies examining passive smoking exposure in patients with pancreatitis due to the need for prospective data collection of this behavioral pattern. A single-center study examining a pediatric pancreatitis population found that of 134 patients, 33 (24.6%) reported outdoor passive smoking exposure while a minority (8.2%) reported indoor passive smoking exposure.[10] Interestingly, this prior study found that indoor passive smoking exposure was associated with a higher rate of hospitalizations, suggesting that passive smoking exposure may play a role in the inflammatory pathway of pancreatitis early in life. A novel finding of our study was the high proportion (62.9%) of patients with pancreatitis (of any form) who had passive smoking exposure, including in nearly half (47.6%) of never-smokers. The extent of

passive smoking among never-smokers, however, did not vary by AP, RAP or CP status. This builds upon the previously seen dose-dependent relationship seen in the development of both AP and CP with individual direct smoking.[4, 19] Given that the median duration of passive smoking exposure ranged 18-20 years in this study, it appears feasible that passive smoking could potentially add to the risk of developing AP and eventually CP. Mouse-model studies also have demonstrated how even low levels of smoking can impair ductal function.[20, 21] However, in never-smokers with CP, we did not observe a difference in patterns of pain or clinical features, except for higher frequency of pancreatic insufficiency. Moreover, the extent of passive smoking across the spectrum of disease (AP, RAP, CP) among never smokers were similar. Thus whether passive smoking exposure should be accounted for in the work-up of patients with pancreatitis remains unclear.[15]

Within the context of CP, the most striking finding of this study was how most patients have sustained tobacco exposure, directly and/or passively. When combined with preclinical data demonstrating the role of smoking in the pathogenesis of CP, these data emphasize the need and opportunity for gastroenterologists to address smoking in patients with pancreatitis. While smoking cessation remains challenging in this patient population, given that the presence of a partner or a household member who smokes makes smoking cessation even more challenging, providers can emphasize to both patients and close contacts the importance of quitting smoking for all parties.[22, 23] At the same time, to better guide future smoking cessation interventions in this population, the mechanism by which smoking damages the pancreas needs continued investigation. For example, if nicotine and its derivates such as nitrosamine 4-(methlnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), are the primary drivers for pancreatic

injury, use of common interventions such as electronic nicotine delivery systems (e.g. E-cigarettes) or nicotine replacement therapy will be of limited value.[24, 25]

In regards to symptoms, pain remains the most debilitating symptom of CP.[26, 27] In a multicenter prospective cohort study (n=1024), the North American Pancreatitis Study 2 (NAPS-2) previously demonstrated that current smoking was associated with worse physical quality of life.[8] This was echoed by the Scandinavian Baltic Pancreatic Club (n=1384) which reported increased odds of painful CP with smoking in a dose-dependent manner.[28] In our study, we similarly found that current smoking was associated with both severe pain and constant pain, two features of pain which have been linked with poor quality of life and higher rates of disability, hospitalizations and opiate use.[27, 29] In light of these findings, further research is needed to determine if smoking cessation will improve both severity and temporality of pain and directly or indirectly improve quality of life in these patients. Additionally, given that patients with CP may smoke to attempt to relieve pain, further studies to determine how smoking affects pain sensation and sensitivity will be insightful.[30]

Prior studies have implicated smoking with accelerated disease progression in CP, primarily in the manifestation of calcifications. A study from Korea examining follow-up imaging studies in patients with CP found that smoking was significantly associated (OR: 9.99) with progression of calcifications.[31] Similarly, a prospective cohort study from Italy found a dose-dependent relationship of smoking with new development of calcifications, finding that 79.1% of current smokers developed calcifications within 5 years of disease onset.[7] This is line with our study which found that 82% of current smokers had calcifications identified on imaging as compared to never-smokers (67%). Our study also found a relatively high rate of pancreatic duct strictures and stones with over half of current smokers having either of the two complications. This

appears consistent with a prior multicenter cross-sectional study (n=1071) from the Scandinavian Baltic Pancreatic Club, which identified three clusters of CP-related complications.[32] Fibrosis-related complications included pancreatic duct strictures and stones, biliary strictures, and duodenal stenosis, with an independent association seen between these complications with smoking (OR: 2.2) and increasing disease duration. Relatedly, this association can help explain why current smoking is a risk factor for receiving pancreatic endotherapy, the primary target of which is treating symptomatic pancreatic duct strictures and stones.[33]

There are several strengths and limitations of this study that warrant further discussion. The strengths of the study include its large sample size, its prospective data collection, and the novel assessment of passive smoking exposure in this population. In terms of limitations, smoking history was self-reported by participants, which is subject to recall bias, but has been shown to be an accurate measure of long-term exposure for both direct and passive smoking.[34, 35] While this study includes data from a control cohort of participants without pancreatitis, a large long-term case-control study would represent an ideal study for the examination of the association between passive smoking exposure and pancreatitis. Additionally, the large number of comparisons (univariate) performed increases the probability of Type 1 error and larger populations will be needed to distinguish the effect of passive smoking from direct smoking. In line with this, cotinine levels were not measured in this cohort, and represents an opportunity for future research to more quantitively assess smoking exposure in patients with pancreatitis.

In summary, passive smoking exposure is highly prevalent in patients with pancreatitis, particularly in those with CP. This further suggests smoking plays a key role in the pathogenesis of CP, but larger, long-term investigations are needed to determine the role of passive smoking exposure in CP pathogenesis. The results of this study also emphasize the critical need to help

patients stop smoking – at all stages within the pancreatitis spectrum. In the future, longer term follow-up from PROCEED and other prospective cohort studies may provide further insights into how smoking and smoking cessation changes the natural history of pancreatitis, including patient-reported outcomes.

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Figure 1: Smoking history categorized by pancreatitis subgroup

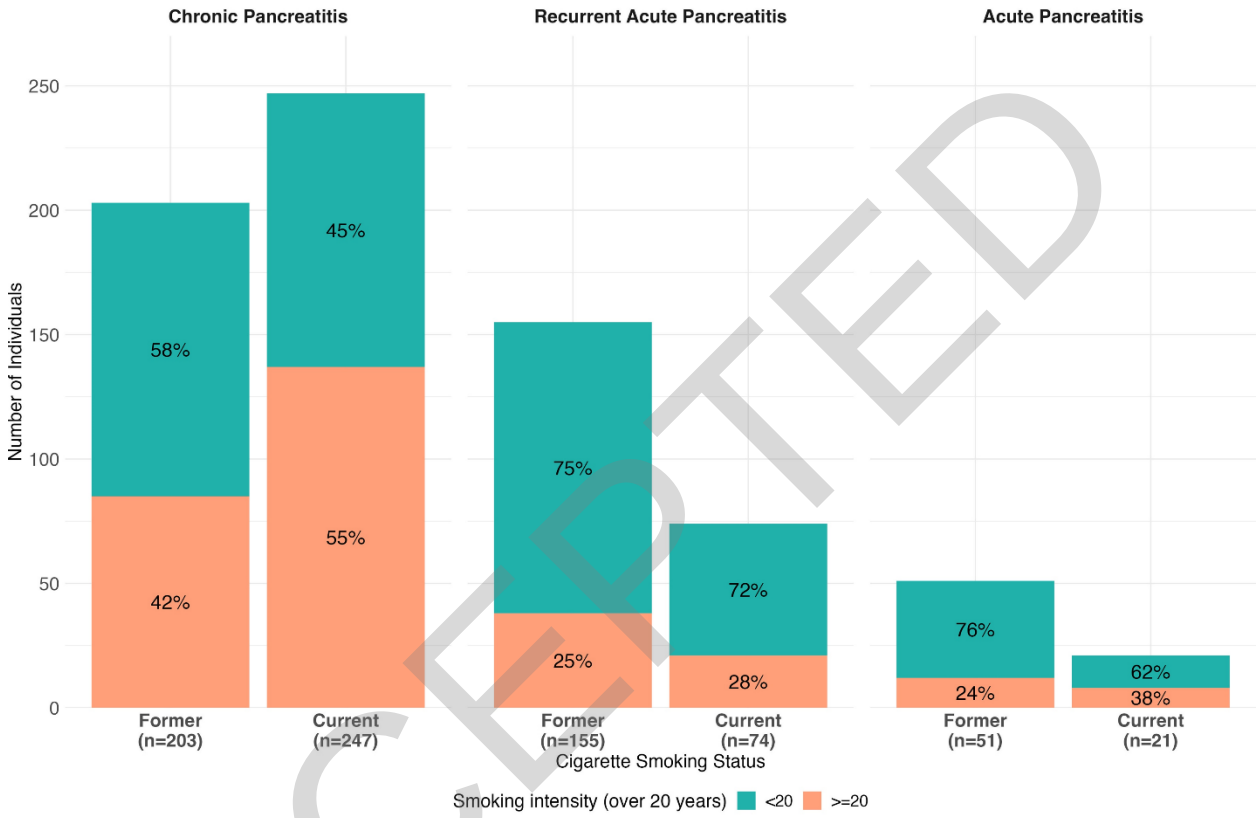

Figure 2: Passive smoking exposure categorized by individual smoking history and pancreatitis subgroup

Table 1: Smoking status and duration by pancreatitis cohort

	Chronic Pancreatitis (N=681)	Recurrent Acute Pancreatitis (N=498)	Acute Pancreatitis (N=190)	P-value
Median Age (IQR)	55.0 (44.0, 63.0)	46.0 (37.0, 57.0)	49.0 (37.0, 60.0)	<.0001[1]
Sex, n (%)				0.7067[2]
Female	317 (46.5%)	241 (48.4%)	94 (49.5%)	
Race, n (%)				0.4440[2]
American Indian/Alaska Native	6 (0.9%)	6 (1.2%)	0 (0.0%)	
Asian	27 (4.0%)	16 (3.2%)	12 (6.3%)	
Black or African American	47 (6.9%)	29 (5.8%)	9 (4.7%)	
Multi-Race	16 (2.3%)	15 (3.0%)	3 (1.6%)	
White	565 (83.0%)	411 (82.5%)	161 (84.7%)	
Other	20 (2.9%)	21 (4.2%)	5 (2.6%)	
Ethnicity, n (%)				0.0005[2]
Hispanic	21 (3.1%)	36 (7.2%)	17 (8.9%)	
Etiology, n (%)				<.0001[2]
Alcohol-related	286 (42.0%)	80 (16.1%)	37 (19.5%)	
Idiopathic	257 (37.7%)	271 (54.6%)	119 (62.6%)	
Other etiology	138 (20.3%)	145 (29.2%)	34 (17.9%)	
Smoking status, n (%)				<.0001[2]
Current	250 (36.7%)	75 (15.1%)	21 (11.1%)	
≥20 pack years of smoking, n (%)*	140 (56.0%)	21 (28.0%)	8 (38.1%)	
Past	203 (29.8%)	155 (31.1%)	51 (26.8%)	
≥20 pack years of smoking**, n (%)	85 (41.9%)	38 (24.5%)	12 (23.5%)	
Never	216 (31.7%)	253 (50.8%)	111 (58.4%)	
Cumulative smoking (pack-years)				<.0001[1]
Median (IQR)	20.0 (8.0, 35.0)	9.0 (3.3, 20.5)	8.0 (3.0, 21.0)	

***% among current smoker; **% among former smoker; [1]Kruskal-Wallis p-value; [2]Chi-Square p-value; IQR: interquartile range**

Table 2: Passive smoking exposure

Smoking status on enrollment	History of passive smoking exposure n (%)	Duration of passive smoking exposure, median years (Q1, Q3)	Number of individuals of exposure to passive smoking
Chronic Pancreatitis (n=681)			
All participants	467 (68.6%)	18.0 (11.5, 30.0)	1: 282 (41.4%) 2: 129 (18.9%) >2: 57 (8.4%)
Current Smoker (n=250)	213 (85.2%)	20.00 (11.00, 36.00)	1: 118 (47.2%) 2: 59 (23.6%) >2: 36 (14.4%)
Former Smoker (n=203)	149 (73.4%)	18.00 (12.00, 25.00)	1: 97 (47.8%) 2: 41 (20.2%) >2: 11 (5.4%)
Never-Smoker (n=216)	105 (48.6%)	18.00 (11.00, 20.00)	1: 67 (31.0%) 2: 29 (13.4%) >2: 10 (4.6%)
Recurrent Acute Pancreatitis (n=498)			
All participants	290 (58.2%)	18.0 (11.0, 22.0)	1: 170 (34.1%) 2: 73 (14.7%) >2: 45 (9.0%)
Current Smoker (n=75)	61 (81.3%)	20.0 (14.5, 33.0)	1: 34 (45.3%) 2: 11 (14.7%) >2: 15 (20.0%)
Former Smoker (n=155)	112 (72.3%)	18.0 (9.5, 23.0)	1: 68 (43.9%) 2: 28 (11.6%) >2: 16 (10.3%)
Never-Smoker (n=253)	117 (46.2%)	18.0 (11.0, 19.0)	1: 68 (26.9%) 2: 34 (13.4%) >2: 14 (5.5%)
Acute Pancreatitis (n=190)			
All participants	105(55.3%)	18.0 (10.0, 21.0)	1: 68 (35.8%) 2: 29 (15.3%) >2: 7 (3.7%)
Current Smoker (n=21)	17 (81.0%)	18.0 (10.0, 21.0)	1: 11 (52.3%) 2: 4 (19.0%) >2: 1 (4.8%)
Former Smoker (n=51)	37 (72.5%)	18.0 (7.0, 20.0)	1: 24 (47.1%) 2: 9 (17.6%) >2: 4 (7.8%)

Never-Smoker (n=111)	51 (45.9%)	18.0 (13.0, 22.0)	1: 33 (29.7%) 2: 16 (14.4%) >2: 2 (1.8%)

Table 3: Comparison of clinical characteristics by smoking status in participants with chronic pancreatitis

Variable	Never-smoker	Former smoker	Current smoker	p value
Pain Severity				
None	38 (17.6%)	32 (15.8%)	30 (12.0%)	0.0019
Mild to moderate	67 (31.0%)	61 (30.0%)	51 (20.4%)	
Severe	109 (50.5%)	109 (53.7%)	164 (65.6%)	
Pain temporality				
Intermittent	104 (48.1%)	83 (40.9%)	86 (34.4%)	0.0006
Constant	72 (33.3%)	87 (42.9%)	129 (51.6%)	
Pancreatic calcifications on imaging	143 (66.5%)	154 (75.9%)	205 (82.0%)	0.002
Pancreatic size (based on parenchymal thickness)				
No atrophy	105 (48.6%)	107 (52.7%)	113 (45.2%)	0.0817
7-14 mm	72 (33.3%)	72 (35.5%)	111 (44.4%)	
< 7 mm	37 (17.1%)	24 (11.8%)	25 (10.0%)	
Pancreatic duct stricture	90 (41.7%)	100 (49.3%)	133 (53.2%)	0.001
Pancreatic duct stone	76 (35.2%)	77 (37.9%)	134 (53.6%)	<0.001
Disease duration in years (median, IQR)	5.0 (1.0, 11.0)	4.0 (1.0, 9.0)	4.0 (1.0, 9.0)	0.1950

IQR: interquartile range

Table 4: Comparison of clinical characteristics by level of passive smoking exposure in never-smokers with chronic pancreatitis

Variable	No passive smoking exposure	<20 years of passive smoking exposure	20+ years of passive smoking exposure	p value
Pain severity				
None	21 (19.1%)	13 (18.6%)	4 (11.4%)	0.82
Mild to moderate	34 (30.9%)	20 (28.6%)	12 (34.3%)	
Severe	54 (49.1%)	36 (51.4%)	19 (54.3%)	
Pain temporality				
Never	21 (19.1%)	13 (18.6%)	4 (11.4%)	0.56
Intermittent	57 (51.8%)	29 (41.4%)	17 (48.6%)	
Constant	31 (28.2%)	27 (38.6%)	14 (40.0%)	
Pancreatic size (based on parenchymal thickness)				
No atrophy	56 (50.91%)	33 (47.14%)	15 (42.86%)	0.77
7-14 mm	33 (30.00%)	27 (38.57%)	12 (34.29%)	
< 7 mm	20 (18.18%)	9 (12.86%)	8 (22.86%)	
Disease duration in years (median, IQR)	6.0 (2.0, 14.0)	5.5 (1.0, 11.0)	2.0 (0.0, 5.0)	0.0234
Pancreatic duct stricture	44 (40.00%)	32 (45.71%)	14 (40.00%)	0.87
Pancreatic duct stone	40 (36.36%)	20 (28.57%)	16 (45.71%)	0.48
Pancreatic calcifications on imaging	76 (69.09%)	42 (60.00%)	25 (71.43%)	0.36
Pancreatic exocrine dysfunction	35 (31.82%)	26 (37.14%)	23 (65.71%)	0.006

IQR: interquartile range