

HHS Public Access

Author manuscript *Pancreatology*. Author manuscript; available in PMC 2019 April 01.

Published in final edited form as:

Pancreatology. 2018 April; 18(3): 269–274. doi:10.1016/j.pan.2018.02.012.

Quality of Life Comparison between Smokers and Non-Smokers with Chronic Pancreatitis

Samuel Han, MD,

Division of Gastroenterology and Hepatology, University of Colorado Anschutz Medical Center, Aurora, Colorado

Boskey Patel, DO,

Department of Internal Medicine, University of Massachusetts Medical Center, Worcester, Massachusetts

May Min, MD,

Department of Internal Medicine, University of Massachusetts Medical Center, Worcester, Massachusetts

Lisa Bocelli, DO,

Division of Gastroenterology, University of Massachusetts Medical Center, Worcester, Massachusetts

Joan Kheder, MD,

Division of Gastroenterology, University of Massachusetts Medical Center, Worcester, Massachusetts

Amy Wachholtz, PhD, and

Department of Psychology, University of Colorado, Denver, Colorado

Wahid Wassef, MD

Division of Gastroenterology, University of Massachusetts Medical Center, Worcester, Massachusetts

Abstract

Objectives—The aim of this study was to evaluate the impact of smoking on quality of life in patients with chronic pancreatitis.

Methods—This is a cross-sectional study of chronic pancreatitis patients followed at a single institution comparing smokers with non-smokers. The primary outcome was quality of life and secondary outcomes included demographics, drug and alcohol use, anxiety and depression, pain level, nutritional status, and metabolic factors.

Results—48 smokers and 45 non-smokers participated in this study. Smokers had a worse overall quality of life and higher rates of opioid addiction and depression than non-smokers. Smokers also

Corresponding Author: Samuel Han, Division of Gastroenterology and Hepatology, University of Colorado Anschutz Medical Center, Mail Stop F735, 1635 Aurora Court, Room 2.031, Aurora, CO 80045, USA, Telephone: 720-848-2777, Fax: 820-848-2749, samuel.han@ucdenver.edu.

Conflicts of Interest: None

had less racial diversity, lower education levels, and higher amounts of narcotic use than nonsmokers. Furthermore, smokers had a lower BMI and a higher proportional use of pancreatic enzyme replacement therapy. Smoking was found to be independently associated with worse quality of life on multivariable regression.

Conclusions—The worse overall quality of life and higher rates of depression and anxiety create cause for concern in chronic pancreatitis patients who smoke. Smoking cessation should be an important target in chronic pancreatitis patients. Multicenter, multiethnic studies are needed to further elucidate this relationship.

Keywords

Chronic pancreatitis; smoking; opioid addiction; quality of life

Introduction

Smoking continues to draw attention for its harmful role in chronic pancreatitis. Smoking is a clear risk factor for the progression of acute pancreatitis to chronic pancreatitis in a dosedependent manner [1, 2]. Furthermore, once chronic pancreatitis develops, smoking can increase the formation of complications such as pancreatic calcifications, exocrine insufficiency, and pseudocysts, indicating its propensity to accelerate disease progression [3-5].

Studies have demonstrated that a high proportion of patients with chronic pancreatitis smoke, but little is known regarding the effects of smoking on quality of life in patients with chronic pancreatitis [6–8]. As there now exists a validated instrument specifically designed to evaluate the quality of life in this patient population, the primary aim of this study was to compare quality of life between smokers and never-smokers with chronic pancreatitis.

Materials and Methods

This is a cross-sectional study within a prospectively collected cohort of patients, approved by our institutional review board. Recruiting was performed from patients with chronic pancreatitis who met the inclusion criteria outlined in Table 1. If patients agreed to participate, they were seen after their regularly scheduled follow-up visit at our chronic pancreatitis clinic. During that visit, an informed consent was signed, a series of questionnaires (detailed below) were given, and blood was drawn for laboratory studies (discussed below). All recruiting was done by two physicians (LB, WW) who primarily follow chronic pancreatitis patients at our tertiary academic medical center. Smokers were self-identified by patients who smoked 1 or more cigarettes a day. Only current smokers and those who never smoked were enrolled in this study, previous smokers were not included.

Demographics form

A demographics form which included standard variables such as age, gender, and race was completed by each patient. It also included socioeconomic variables such as education level, marital status, and employment status. Medication use was also documented, including the

use and dosage of pain medications, antidepressants, diabetes medications, pancreatic enzyme supplementation, and nutritional supplements.

Questionnaires

A series of validated questionnaires were given to every patient and these included: 1) the PANcreatitis Quality Of Life Instrument (PANQOLI) [9], a questionnaire specifically designed to assess quality of life in chronic pancreatitis populations, 2) the Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R) [10], which assesses the potential for opioid addiction, 3) the Drug Alcohol Screening Test (DAST) [11], which screens for drug abuse misuse, 4) the Michigan Alcohol Screening Test (MAST) [12] which detects alcoholism 5) the Brief Cope 24 which measures coping skills [13], 6) the Hospital Anxiety and Depression Scale (HADS) [14] which detects depression and anxiety, 7) the Malnutrition Universal Screening Test (MUST) [15] which evaluates for malnutrition, and 8) the Visual Analog Scale (VAS) which was used to determine the patient's level of pain.

Laboratory and Endoscopy Data

All patients had laboratory data collected to assess for nutritional and metabolic factors including Vitamin A, Vitamin D, Vitamin E, Vitamin K, prothrombin time, magnesium, calcium, albumin, prealbumin, and triglyceride levels (hypertriglyceridemia defined as a serum triglyceride level 200) [16]. Secretin stimulation testing was done as previously described and peak bicarbonate levels were measured for patients [17]. All patients received endoscopic ultrasound (EUS) for confirmation of chronic pancreatitis and disease severity was graded as previously described using number of EUS criteria (hyperechoic foci, hyperechoic strands, lobularity, hyperechoic duct, irregular duct, visible side branches, ductal dilation, calcification, and cysts) present [18, 19].

Statistical Analysis

Continuous values were reported as mean \pm SD. Statistical analysis was performed using Fisher's exact test for categorical variables and Student's t-test for continuous variables in comparing the two groups (STATA 14.2, StataCorp, College Station, Texas, USA). Multivariable linear regression analysis was performed to determine independent predictors of quality of life using PANQOLI scores as a marker for quality of life. Independent variables for this analysis included demographic and disease characteristics. A two-sided P value < 0.05 was considered to be significant. No corrections were made for multiple comparisons.

Results

Demographics and Disease Characteristics

A total of 95 patients with chronic pancreatitis were identified in this study, of which two (smokers) were excluded due to the presence of stage IV cancer, leaving 93 patients (48 smokers and 45 non-smokers). The mean age was $48.5 (\pm 10.5)$ years, 59 (63.4%) were female, and 78 (88.6%) were Caucasian. Smokers were significantly less heterogeneous in terms of race than non-smokers with non-smokers having more African-American and Hispanic patients (p=0.02) (Table 2). They were less-educated than non-smokers (p=0.004)

and there was no significant difference in chronic pancreatitis etiology between the two groups. Overall, there was no significant difference in disease severity as measured by EUS findings between the two groups, but the smoking group had a higher proportion of patients with severe disease (25% vs. 6.7%, p=0.02). The smoking group had on average a 25.5 pack-year history and currently smoked 0.7 packs (14 cigarettes)/day.

Quality of Life

Smokers had a worse overall quality of life on the PANQOLI compared to non-smokers $(50.3 \pm 9.6 \text{ vs.} 59.3 \pm 16.2, \text{ respectively, p=0.003})$, a higher potential for opioid abuse in terms of the SOAPP-R (p=0.02), and higher rates of depression and anxiety based on the HADS score (p=0.005), but better coping skills on the Brief Cope 24 (p=0.009) (Table 3). Multivariate analysis included demographic variables, smoking status, and chronic pancreatitis duration, severity and etiology. This regression revealed that quality of life based on the PANQOLI was only significantly associated with smoking with a parameter estimate or a coefficient of -8.6, suggesting an inverse relationship of smoking with quality of life (p=0.008) (Table 4).

Nutritional and Metabolic Factors

Amongst the nutritional and metabolic factors (Table 5), smokers had a significantly lower body mass index (BMI) than non-smokers (24.1 vs. 28.7, p=0.002), and a higher proportion of patients with low pre-albumin levels than non-smokers (40% vs. 20.8%, p=0.04).

Medications

Medication use data (Table 6) displayed that a higher proportion of smokers used narcotics for pain control (95.8% vs. 71.1%, p=0.001) and required pancreatic enzyme replacement therapy (95.8% vs. 73.3%, p=0.002) compared to non-smokers. There was no difference between smokers and non-smokers however in daily dose of opiates quantified in morphine equivalents (210.2 in smokers vs. 155.6 mg/day in non-smokers, p=0.12).

Discussion

Numerous studies have demonstrated that smoking is a clear risk factor for both acute and chronic pancreatitis, accelerating disease progression, both from acute pancreatitis to chronic pancreatitis but also within chronic pancreatitis [1, 2, 6, 20–22]. Smoking has indeed been shown to be associated with calcification development, exocrine insufficiency, pseudocyst development, and severe morphologic changes in chronic pancreatitis [4, 5]. However, few studies have directly compared its impact on quality of life in chronic pancreatitis patients. One of the remarkable aspects of chronic pancreatitis is the high prevalence of smoking as the North American Pancreatitis Study 2 (NAPS2) found that 47.3% of their chronic pancreatitis patients were current smokers, while 71.4% had smoked during at least one point in their life [6]. Similarly, a Japanese study found that 44.9% of their patients were current smokers and 74.6% were ever smokers [7].

Using the PANQOLI, the first validated instrument that was designed specifically for the evaluation of quality of life in chronic pancreatitis, we found that smokers had a worse

quality of life in all functions, including physical function, role function, emotional function and self-worth. Our study also indicated that smokers had higher potential for opioid abuse, depression, and anxiety, based on the SOAPP-R and HADS questionnaires respectively. These findings seem to be compatible with those of the NAPS2 study which had previously demonstrated that chronic pancreatitis patients do indeed have a worse quality of life compared to a healthy population based on the Short Form-12, a generalized quality of life instrument that offers an evaluation of physical health and mental health [23]. A recent study by Machicado et al combined all three of the NAPS2 studies and found that based on using the Short-Form-12 as a measure of quality of life, factors including constant pain, painrelated disability/unemployment, current smoking, and concurrent co-morbidities significantly affected quality of life in this patient population [24]. Specifically, constant pain had the largest impact on physical quality of life, followed by disability/unemployment and then current smoking, with the interesting finding that subjects with a moderate or heavy drinking history had improved physical quality of life compared to subjects who were lifelong abstainers. Similarly, in terms of mental quality of life, constant pain also had the largest impact, followed by current smoking and disability/unemployment. Multivariable analysis in our study demonstrated that smoking status was the primary independent variable associated with worse PANQOLI scores.

There were a variety of differences between smokers and non-smokers in this study that warrant attention. In terms of demographics, while there were no differences in age or gender, there was more racial diversity in the non-smoking group. It is unclear as to what role this may play in interpreting these results given the particularly small number of non-Caucasians in both groups, which reflects the patient population of our medical center. Further multi-ethnic studies will need to be done to elucidate the differences between races in this disease. Smokers also had significantly lower education levels, with non-smokers having more patients with college degrees (37.8% vs. 10.4%, p=0.004). This appears to be in line with the general population as the Centers for Disease Control (CDC) has reported decreasing smoking rates with higher levels of education [25]. While not statistically different, 60% of smokers were also unemployed, compared to 40% in non-smokers, which in combination with education level may reflect the socioeconomic background of smokers.

In terms of nutritional and metabolic factors, smokers had a lower BMI and a greater proportion of smokers had low prealbumin levels compared to non-smokers. The lower BMI is expected with smokers given the association of smoking with decreased food intake and increased energy expenditure [26, 27]. While no clear relationship between smoking and prealbumin levels exists, the lower prealbumin may hint at differences in nourishment between smokers and non-smokers, despite the lack of difference in rate of malnourishment based on screening via the MUST.

Smokers, as expected, had a significantly higher rate of narcotic use than non-smokers given the common occurrence of co-addictions. A higher proportion of smokers also required pancreatic enzyme replacement therapy, which is in line with the known disease acceleration in chronic pancreatitis caused by smoking. Interestingly, there was no difference in bicarbonate secretion between the two groups, but pancreatic enzyme supplementation was prescribed based on symptoms, specifically steatorrhea and diarrhea, which may not

correlate precisely with bicarbonate secretion. Another interesting finding was the high use of antidepressants as nearly 50% of smokers and non-smokers reported taking antidepressants, which further speaks to the prevalence of depression and poor quality of life experienced by these patients.

Previous studies have demonstrated the disease acceleration caused by smoking, which would in turn be expected to result in greater disease severity in the smoking group [4, 5]. There were no significant differences, however, in disease severity based on EUS findings between the smoking and non-smoking groups, although the smoking group did have a higher proportion of patients with severe disease compared to the non-smoking group. As mentioned above, there was also no difference in bicarbonate secretion on secretin pancreatic function testing between the two groups but several studies have previously demonstrated the suboptimal concordance and correlation of EUS with direct pancreatic function testing [28-30]. Finally, the smoking group did have a higher requirement of pancreatic enzyme replacement therapy, which would imply greater disease severity if using clinical criteria as in the M-ANNHEIM clinical staging system [31]. While not definitive, the higher proportion of severe disease coupled with the greater use of enzyme replacement therapy in the smoking group hints at a worse disease state in the smoking group, which may also be contributing to a worse quality of life.

Taken together, smoking in chronic pancreatitis appears to have a significant negative effect on quality of life in patients with chronic pancreatitis. Within quality of life, anxiety and depression in particular warrant particular attention and physicians must be vigilant in monitoring for these conditions given the danger of mental health deterioration. Smokers also likely represent a less-educated, under-employed socioeconomic status, which highlight the particular struggles these patients may be going through. The lower BMI, low prealbumin proportion, and high proportion of enzyme replacement therapy use in smokers hint at malnourishment in this subgroup, which may not even be detected by typical screening methods. Lastly, smokers are likely to exhibit co-addiction with opiates, stressing the importance of careful monitoring of opiate use in this subgroup of patients, particularly given the current opiate epidemic in the United States [32].

There are several limitations to this study. In addition to the limitations inherent to a crosssectional design, this study population is small and limited to a single-center, representative of a specific geographic area and population. This is seen in the gender composition of the entire cohort, as females represented 62.4% of the group, which is higher than the 46.7% seen in the NAPS2 population [23]. Additionally, it is difficult to determine a temporal relationship between smoking and quality of life from this study. Similar to how Setiawan et al analyzed the effects of drinking and smoking in acute pancreatitis in their multiethnic cohort [22], a multi-center, multi-ethnic prospective database study could help elucidate the long-term effects of smoking while also delineating between racial differences. Lastly, confounding variables are always of concern, which necessitated the use of multivariate regression to help clarify the relationship of smoking with quality of life. Looking at disease severity as a potential confounding variable, while there was no significant association with quality of life and EUS-based disease severity on multivariate analysis, as discussed above, there are several findings that suggest that the smoking group had clinically greater disease

severity, which may affect quality of life as well. Multivariable regression is weakened by including numerous variables, particularly with a small sample size, and future studies will need to investigate this relationship.

In summary, this study provides a comprehensive comparison of smokers and never-smokers with chronic pancreatitis and highlights the negative influence of smoking on quality of life. The next step will be to assess whether quality of life improves after smoking cessation. Unfortunately, as has been previously demonstrated, smoking is extremely difficulty in this population and innovative, effective strategies will be needed to help these patients quit smoking [8]. In the meantime, it becomes paramount for pancreatologists to be mindful of quality of life factors such as depression, anxiety, nutrition, and opiate use to provide comprehensive care in this difficult population.

Acknowledgments

None

Funding: S.H was supported by NIH T32DK007038-42

References

- Rebours V, Vullierme MP, Hentic O, Maire F, Hammel P, Ruszniewski P, et al. Smoking and the course of recurrent acute and chronic alcoholic pancreatitis: a dose-dependent relationship. Pancreas. 2012; 41(8):1219–24. [PubMed: 23086245]
- Sadr-Azodi O, Andren-Sandberg A, Orsini N, Wolk A. Cigarette smoking, smoking cessation and acute pancreatitis: a prospective population-based study. Gut. 2012; 61(2):262–7. [PubMed: 21836026]
- Sankaran SJ, Xiao AY, Wu LM, Windsor JA, Forsmark CE, Petrov MS. Frequency of progression from acute to chronic pancreatitis and risk factors: a meta-analysis. Gastroenterology. 2015; 149(6): 1490–500.e1. [PubMed: 26299411]
- 4. Greer JB, Thrower E, Yadav D. Epidemiologic and Mechanistic Associations Between Smoking and Pancreatitis. Curr Treat Options Gastroenterol. 2015; 13(3):332–46. [PubMed: 26109145]
- Luaces-Regueira M, Iglesias-Garcia J, Lindkvist B, Castineira-Alvarino M, Nieto-Garcia L, Larino-Noia J, et al. Smoking as a risk factor for complications in chronic pancreatitis. Pancreas. 2014; 43(2):275–80. [PubMed: 24518508]
- 6. Cote GA, Yadav D, Slivka A, Hawes RH, Anderson MA, Burton FR, et al. Alcohol and smoking as risk factors in an epidemiology study of patients with chronic pancreatitis. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 2011; 9(3):266–73. quiz e27. [PubMed: 21029787]
- Hirota M, Shimosegawa T, Masamune A, Kikuta K, Kume K, Hamada S, et al. The seventh nationwide epidemiological survey for chronic pancreatitis in Japan: clinical significance of smoking habit in Japanese patients. Pancreatology : official journal of the International Association of Pancreatology (IAP). 2014; 14(6):490–6. [et al].
- Han S, Kheder J, Bocelli L, Fahed J, Wachholtz A, Seward G, et al. Smoking Cessation in a Chronic Pancreatitis Population. Pancreas. 2016; 45(9):1303–8. [PubMed: 27101574]
- Wassef W, DeWitt J, McGreevy K, Wilcox M, Whitcomb D, Yadav D, et al. Pancreatitis Quality of Life Instrument: A Psychometric Evaluation. The American journal of gastroenterology. 2016; 111(8):1177–86. [PubMed: 27296943]
- Butler SF, Fernandez K, Benoit C, Budman SH, Jamison RN. Validation of the revised Screener and Opioid Assessment for Patients with Pain (SOAPP-R). The journal of pain : official journal of the American Pain Society. 2008; 9(4):360–72. [PubMed: 18203666]

- 11. Skinner HA. The drug abuse screening test. Addictive behaviors. 1982; 7(4):363–71. [PubMed: 7183189]
- 12. Selzer ML. The Michigan alcoholism screening test: the quest for a new diagnostic instrument. The American journal of psychiatry. 1971; 127(12):1653–8. [PubMed: 5565851]
- Carver CS. You want to measure coping but your protocol's too long: consider the brief COPE. International journal of behavioral medicine. 1997; 4(1):92–100. [PubMed: 16250744]
- Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta psychiatrica Scandinavica. 1983; 67(6):361–70. [PubMed: 6880820]
- 15. Weekes CE, Elia M, Emery PW. The development, validation and reliability of a nutrition screening tool based on the recommendations of the British Association for Parenteral and Enteral Nutrition (BAPEN). Clinical nutrition (Edinburgh, Scotland). 2004; 23(5):1104–12.
- Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation. 2002; 106(25):3143–421. [PubMed: 12485966]
- Conwell DL, Zuccaro G Jr, Vargo JJ, Trolli PA, Vanlente F, Obuchowski N, et al. An endoscopic pancreatic function test with synthetic porcine secretin for the evaluation of chronic abdominal pain and suspected chronic pancreatitis. Gastrointestinal endoscopy. 2003; 57(1):37–40. [PubMed: 12518128]
- Irisawa A, Katakura K, Ohira H, Sato A, Bhutani MS, Hernandez LV, et al. Usefulness of endoscopic ultrasound to diagnose the severity of chronic pancreatitis. Journal of gastroenterology. 2007; 42(Suppl 17):90–4. [PubMed: 17238035]
- Sahai AV, Zimmerman M, Aabakken L, Tarnasky PR, Cunningham JT, van Velse A, et al. Prospective assessment of the ability of endoscopic ultrasound to diagnose, exclude, or establish the severity of chronic pancreatitis found by endoscopic retrograde cholangiopancreatography. Gastrointestinal endoscopy. 1998; 48(1):18–25. [PubMed: 9684659]
- Munigala S, Conwell DL, Gelrud A, Agarwal B. Heavy Smoking Is Associated With Lower Age at First Episode of Acute Pancreatitis and a Higher Risk of Recurrence. Pancreas. 2015; 44(6):876– 81. [PubMed: 25906444]
- 21. Ahmed Ali U, Issa Y, Hagenaars JC, Bakker OJ, van Goor H, Nieuwenhuijs VB, et al. Risk of Recurrent Pancreatitis and Progression to Chronic Pancreatitis After a First Episode of Acute Pancreatitis. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 2016; 14(5):738–46. [PubMed: 26772149]
- Setiawan VW, Pandol SJ, Porcel J, Wilkens LR, Le Marchand L, Pike MC, et al. Prospective Study of Alcohol Drinking, Smoking, and Pancreatitis: The Multiethnic Cohort. Pancreas. 2016; 45(6): 819–25. [PubMed: 27171516]
- Amann ST, Yadav D, Barmada MM, O'Connell M, Kennard ED, Anderson M, et al. Physical and mental quality of life in chronic pancreatitis: a case-control study from the North American Pancreatitis Study 2 cohort. Pancreas. 2013; 42(2):293–300. [PubMed: 23357924]
- Machicado JD, Amann ST, Anderson MA, Abberbock J, Sherman S, Conwell DL, et al. Quality of Life in Chronic Pancreatitis is Determined by Constant Pain, Disability/Unemployment, Current Smoking, and Associated Co-Morbidities. The American journal of gastroenterology. 2017; 112(4):633–42. [PubMed: 28244497]
- CDC. Current Cigarette Smoking Among Adults Aged 18 Years —United States, 2009. MMWR Morbidity and mortality weekly report. 2010; 59:1135–40. [PubMed: 20829747]
- Filozof C, Fernandez Pinilla MC, Fernandez-Cruz A. Smoking cessation and weight gain. Obesity reviews : an official journal of the International Association for the Study of Obesity. 2004; 5(2): 95–103. [PubMed: 15086863]
- Leslie WS, Koshy PR, Mackenzie M, Murray HM, Boyle S, Lean ME, et al. Changes in body weight and food choice in those attempting smoking cessation: a cluster randomised controlled trial. BMC public health. 2012; 12:389. [PubMed: 22642755]
- Stevens T, Dumot JA, Parsi MA, Zuccaro G, Vargo JJ. Combined endoscopic ultrasound and secretin endoscopic pancreatic function test in patients evaluated for chronic pancreatitis. Digestive diseases and sciences. 2010; 55(9):2681–7. [PubMed: 20101462]

- 29. Catalano MF, Lahoti S, Geenen JE, Hogan WJ. Prospective evaluation of endoscopic ultrasonography, endoscopic retrograde pancreatography, and secretin test in the diagnosis of chronic pancreatitis. Gastrointestinal endoscopy. 1998; 48(1):11–7. [PubMed: 9684658]
- Chowdhury R, Bhutani MS, Mishra G, Toskes PP, Forsmark CE. Comparative analysis of direct pancreatic function testing versus morphological assessment by endoscopic ultrasonography for the evaluation of chronic unexplained abdominal pain of presumed pancreatic origin. Pancreas. 2005; 31(1):63–8. [PubMed: 15968249]
- Schneider A, Lohr JM, Singer MV. The M-ANNHEIM classification of chronic pancreatitis: introduction of a unifying classification system based on a review of previous classifications of the disease. Journal of gastroenterology. 2007; 42(2):101–19. [PubMed: 17351799]
- 32. Unger JR. Staring down the opioid epidemic. The Journal of family practice. 2017; 66(1):8. [PubMed: 28188310]

Inclusion - Exclusion Criteria

Inclusion criteria		Exclusion criteria	
Patient must have one of the following two features:		Patient to be excluded from the study if they have one of the following	
a.	Presence of pancreatic calcification as demonstrated by CT scan or KUB imaging	a. Age less than 18 years	
b.	Presence of five out of nine criteria of pancreatic injury by endoscopic ultrasound in conjunction with a positive secretin stimulation test to confirm pancreatic insufficiency.	b.	Comorbidities including end-stage cancer (estimated survival < 6 months), HIV (T4 cell count < 50), end-stage congestive heart failure, end-stage chronic obstructive pulmonary disease, uncompensated cirrhosis, renal failure (on dialysis or with CrCl <25), or pre-existing diabetes mellitus
		c.	Prisoners
		d.	Non-English speaking
		e.	Former smokers

CT: computed tomography; KUB: kidney, ureter, and bladder; CrCl: creatinine clearance

Comparison of Demographics and Disease Characteristics between Current Smokers and Non-smokers

	Current Smoker (n=48) Mean (SD) or N (%)	Non-Smoker (n=45) Mean (SD) or N (%)	P valu
Age	47.1 ± 9.9	51.0 ± 10.4	0.08
Gender			0.97
Females	30 (62.5%)	n=28 (62.2%)	
Males	18 (37.5%)	n=17 (37.8%)	
Race			0.02
Caucasian	46 (95.7%)	36 (80%)	
African-American	0 (0%)	5 (11.1%)	
Hispanic	0 (0%)	3 (6.7%)	
Mixed	2 (4.2%)	1 (2.2%)	
Marital Status			0.19
Married	18 (37.5%)	17 (37.8%)	
Divorced	13 (27.1%)	5 (11.1%)	
Single	9 (18.8%)	11 (24.4%)	
Single Parent	6 (12.5%)	5 (11.1%)	
Unmarried	1 (2.1%)	6 (13.3%)	
Widowed	1 (2.1%)	1 (2.2%)	
Education Level			0.004
Less than high school	6 (12.5%)	2 (4.4%)	
High school graduate	33 (68.8%)	17 (37.8%)	
Some college	4 (8.3%)	6 (13.3%)	
Associate's Degree	0 (0%)	2 (4.4%)	
Bachelor's Degree	5 (10.4%)	17 (37.8%)	
Graduate degree	0 (0%)	1 (2.2%)	
Employment Status			0.2
Employed	13 (27.1%)	16 (35.6%)	
Unemployed	29 (60.4%)	18 (40%)	
Retired	1 (2.1%)	3 (6.7%)	
On Disability	5 (10.4%)	8 (17.8%)	
Past Addictions	30 (62.5%)	23 (56.1%)	0.27
Disease duration (years)	4.1 ± 3.4	4.4 ± 5.2	0.36
Etiology			0.21
Alcohol	20 (41.7%)	15 (33.3%)	
Ductal Obstruction	10 (20.8%)	3 (6.7%)	
-IPMN	5 (10.4%)	1 (2.2%)	

	Current Smoker (n=48) Mean (SD) or N (%)	Non-Smoker (n=45) Mean (SD) or N (%)	P value
-Anastomotic Stricture	4 (8.3%)	1 (2.2%)	
-Trauma	1 (2.1%)	1 (2.2%)	
Hereditary	5 (10.4%)	7 (15.6%)	
Autoimmune	2 (4.2%)	1 (2.22%)	
Cystic Fibrosis	1 (2.1%)	2 (4.44%)	
Idiopathic	10 (20.8%)	17 (37.8%)	
Severity (based on EUS findings)			0.2
Mild	10 (20.8%)	12 (26.7%)	
Mild-moderate	5 (10.4%)	7 (15.6%)	
Moderate	17 (35.4%)	18 (40%)	
Moderate-severe	4 (8.3%)	5 (11.1%)	
Severe	12 (25%)	3 (6.7%)	
Pack-years	25.5 ± 17.3	-	-
Current packs/day	0.7 ± 0.4	_	_

Comparison of Quality of Life between Current Smokers and Non-Smokers

	Current Smoker Mean (SD)	Non-Smoker Mean (SD)	P value
Pancreatitis Quality of Life Instrument (PANQOLI)	50.3 ± 9.6	59.3 ± 16.2	0.003
Michigan Alcohol Screening Test (MAST)	2.8 ± 3.5	1.3 ± 1.5	0.08
Drug Alcohol Screening Test (DAST)	2.6 ± 1.6	2.3 ± 1.9	0.32
Brief Cope 24	103.1 ± 14.8	84 ± 31.4	0.009
Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R)	19.2 ± 10.4	13.8 ± 7.3	0.02
Hospital Anxiety and Depression Scale (HADS)	18.3 ± 8.4	12.5 ± 7.1	0.005
Visual Analog Scale (VAS) for pain	49.2 ± 22.7	47.8 ± 25.8	0.4
Malnutrition Universal Screening Test (MUST)	0.8 ± 1.3	0.6 ± 1.2	0.1

Multivariable Regression of demographic variables in relation to Quality of Life as determined by the PANQOLI

Variable	Reference Variable	Parameter estimate (95% CI)	Standard Error	P value
Age	-	-0.16 (-0.5,0.2)	0.16	0.14
Male gender	Female gender	4.5 (-1.7, 10.7)	3.0	0.15
Current Smoking	Non-Smoking	-8.6 (-15.9, -1.1)	3.5	0.008
Packs of cigarettes/day	-	-1.5 (-10.5, 7.4)	4.2	0.91
Pack-years	-	-0.01 (-0.3, 0.3)	0.13	0.72
Alcohol etiology	Non-alcohol etiologies	-4.9 (-13.9, 4.1)	4.4	0.28
High school level education	College education	-2.3 (-12.4, 7.9)	5.0	0.13
Caucasian race	All other races	2.3 (-12.1, 16.7)	7.1	0.74
Divorced	Married	-0.9 (-8.3, 6.6)	3.8	0.82
Unemployed	Employed	-4.9 (-13.6, 3.6)	4.3	0.25
Chronic Pancreatitis duration	-	0.15 (-0.5, 0.8)	0.39	0.63
Severe disease severity (based on EUS)	Mild disease severity	1.9 (-11.7, 15.5)	6.7	0.8

R²=0.69, p=0.0005

Comparison of Nutritional and Metabolic risk factors between Current Smokers and Nonsmokers

	Current Smoker (n=48) Mean (SD) or N (%)	Non-Smoker (n=45) Mean (SD) or N (%)	P value
BMI	24.1 a 6.2	28.7 a 8.8	0.002
Vitamin A level (µg/dL)	47.9 ± 18.1	58.9 ± 37.8	0.08
Vitamin A deficiency	15 (31.3%)	20 (44.4%)	0.18
Vitamin D level (ng/mL) Vitamin D deficiency	26.3 ± 12.2 32 (66.7%)	29.9 ± 15.4 26 (57.8%)	0.11 0.37
Vitamin E level (µg/mL) Vitamin E deficiency	10.6 ± 5.2 13 (37.1%)	12.6 ± 5.9 6 (15.4%)	0.09 0.1
Vitamin K level (ng/mL) Vitamin K deficiency	2.4 ± 1.2 11 (22.9%)	2.6 ± 1.3 10 (22.2%)	0.25 0.9
Prothrombin time (sec)	11.9 ± 4.1	10.9 ± 7.3	0.29
Magnesium level (mEq/L) Hypomagnesemia	$\begin{array}{c} 1.0 \pm 0.2 \\ 3 \ (6.3\%) \end{array}$	2.0 ± 0.5 7 (15.6%)	0.19 0.14
Calcium level (mg/dL) Hypocalcemia	9.0 ± 1.2 8 (16.7%)	8.5 ± 1.5 15 (33.3%)	0.15 0.06
Albumin (g/dL)	4.0 ± 0.6	3.9 ± 0.7	0.29
Hypoalbuminemia	10 (20.8%)	10 (22.2%)	0.86
Prealbumin level (mg/dL)	19 ± 10.4	21.5 ± 6.3	0.16
Low prealbumin level	18 (40%)	10 (20.8%)	0.04
Triglyceride level (mg/dL)	167.3 ± 98.3	230.8 ± 220.8	0.08
Hypertriglyceridemia	22 (45.8%)	22 (48.9%)	0.76
Bicarbonate level (peak-mEq/L) during secretin stimulation	68.1 ± 15.3	71.4 ± 20.9	0.38

Comparison of Medications between Current Smokers and Non-smokers

	Current Smoker (n=48) Mean (SD) or N (%)	Non-Smoker (n=45) Mean (SD) or N (%)	P value
Narcotic Use	46 (95.8%)	32 (71.1%)	0.001
Morphine equivalents (mg/day)	210.2 ± 161.2	155.6 ± 148.6	0.12
Multivitamin use	12 (25.0%)	10 (22.2%)	0.75
Insulin use	6 (12.5%)	6 (13.3%)	0.9
Oral hypoglycemic use	3 (6.3%)	5 (11.1%)	0.4
Pancreatic enzyme replacement therapy Lipase (units) Protease (units) Amylase (units)	$46 (95.8\%)$ $135,000 \pm 165,724$ $300,894 \pm 150,866$ $707,188 \pm 149,800$	33 (73.3%) 94,125 ± 44,017 297,000 ± 139,957 473,125 ± 220,126	0.002
Antidepressant use	24 (50%)	22 (48.9%)	0.91
Osteoporosis	2 (4.2%)	0 (0%)	0.16