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# The prevalence of underweight is increased in chronic pancreatitis outpatients and associates with reduced life quality

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ABSTRACT

*Background:* Underweight is a well-known complication of chronic pancreatitis (CP), but little is known about its prevalence in the outpatient setting. We investigated the prevalence of underweight in outpatients with CP and its association with quality of life (QOL) and various risk factors.
*Methods:* This was a cross-sectional study of 166 outpatients with CP that was conducted at a tertiary referral center. The primary outcome was the prevalence of underweight (body mass index [BMI] <20 kg/m$^2$) in patients with CP compared with 160 age- and sex-matched controls. Clinical and demographic parameters including QOL, exocrine pancreatic insufficiency (EPI), pain severity, pain pattern (constant versus intermittent), opioid use, and smoking and drinking habits were analyzed for their association with BMI.
*Results:* Patients with CP had a decreased mean BMI compared with controls (22.9 ± 4.2 kg/m$^2$ versus 26.8 ± 5.2 kg/m$^2$; $P < 0.0001$). Of 166 patients with CP, 43 (26.0% [95% confidence interval: 19.8–33.1%]) were underweight compared with 15 of 160 controls (9.4% [95% confidence interval: 5.8–14.9%]; odds ratio: 3.38 [95% confidence interval: 1.79–6.38]; $P = 0.0001$). Several QOL scales and items were associated with underweight, including physical functioning ($P = 0.024$). Alcoholic etiology ($P = 0.002$), EPI ($P = 0.004$), and constant pain ($P = 0.026$) were independently associated with low BMI.
*Conclusions:* One quarter of outpatients with CP are underweight and report reduced life quality compared with their normal-weight counterparts. EPI, alcoholic etiology, and pain-related symptoms are independent risk factors. Our findings emphasize the need for a multidisciplinary approach in the handling of patients with CP that focuses on alcohol cessation and the appropriate treatment of pain and EPI.

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## Introduction

Chronic pancreatitis (CP) is a fibroinflammatory disease that causes irreversible injury to pancreatic tissue [1]. As the disease evolves, significant impairment of exocrine and endocrine pancreatic functions becomes evident and, in addition to chronic abdominal pain, affects dietary intake, digestion, and absorption of micro- and macronutrients [2]. This may lead to underweight and malnutrition, which has been associated with increased hospitalization frequencies, poor outcome, and high mortality in patients with various chronic diseases [3–8]. However, little is known about this important complication in the context of CP.

Prevalence estimates of underweight and malnutrition in patients with CP have been reported mainly from in-hospital surveys and vary considerably, ranging from 23% to 94% [9–12]. However, because most patients are treated in an outpatient setting, these numbers probably overestimate the

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population-based prevalence by inclusion of patients with more advanced disease, a higher symptom burden, and thus an increased risk of underweight (i.e., selection bias). Also, previous studies did not include a healthy control group; therefore, it is unknown if the prevalence of underweight in patients with CP is increased compared with that observed in healthy controls [9–12].

The risk factors associated with underweight in patients with CP are complex and likely multifactorial with the most frequently reported being exocrine pancreatic insufficiency (EPI) [13,14]. However, many patients lose weight early in their disease course and before evolution of EPI; as such, other factors must be of significance [15,16]. For example, postprandial pain, which is seen in many patients, may also limit food intake and lead to underweight and malnutrition. There is a paucity of data on this important question, and most previous studies did not take multiple risk factors into consideration.

We investigated the prevalence of underweight and its association with quality of life (QOL) and several risk factors in a cohort of well-characterized outpatients with CP. We hypothesized that the prevalence of underweight was increased in patients with CP compared with an age- and sex-matched group of controls and that underweight was associated with reduced QOL as well as multiple risk factors in addition to EPI. The aims of the study were to determine the prevalence of underweight in outpatients with CP, investigate the association between underweight and QOL, and determine the risk factors that are associated with underweight.

## Methods

This was a cross-sectional study conducted at Centre of Pancreatic Diseases, Department of Gastroenterology and Hepatology at Aalborg University Hospital in Denmark from November 2010 through August 2015. Consecutive patients with CP who were referred to our tertiary center, which specializes in the treatment of patients with CP, were included. The diagnosis of CP was based on the modified Mayo Clinic criteria (Lüneburg), and CP was defined as a score of ≥4 points [17]. This system is a modification of the one used at Mayo Clinic [15] and includes indirect pancreatic function tests, ultrasound, magnetic resonance imagining, and computed tomography. The body mass index (BMI) and prevalence of underweight in patients with CP was compared with that observed in an age- and sex-matched cohort of healthy controls without any known pancreatic or gastrointestinal disorders. The local ethics committee approved the protocol (N-20120001).

### *Study outcomes*

The primary study outcome was underweight, defined as a BMI <20.0 kg/m$^2$ in accordance with the recent commenced population-derived estimates from the Global BMI Mortality Collaboration [18]. Secondary outcomes included clinical and demographic risk factors for underweight and their interaction.

### *Quality of life*

The European Organization for Research and Treatment of Cancer, Quality of Life Questionnaire-core 30 was used to evaluate QOL [19]. This questionnaire is composed of single-item measures and multi-item scales with scores that range from 0 to 100 after linear transformation of the raw score. A high score for a functional scale represents a high level of functioning, as does a high score for the global health status, but a high score for the symptom items represents a high level of symptomatology.

### *Risk factors for malnutrition*

A number of risk factors that have been associated previously with underweight and malnutrition in patients with CP and other patient populations were defined pre hoc. In addition to sex and age, these factors included etiology and duration of CP [15,20], alcohol consumption [21,22], smoking habit [21], pain severity and its pattern in time [3,23], opioid treatment [24], exocrine pancreatic insufficiency [15], and diabetes mellitus [15].

Information on patients' demographic characteristics, etiology of CP, exocrine pancreatic insufficiency, diabetes, use of pain medications, alcohol consumption, and smoking habits were collected in standardized case report forms. Patients with alcohol consumption that was above the safe limits recommended by the Danish Health and Medicines Authorities (i.e., >7 units of alcohol per week for women and >14 units for men) were categorized as excessive alcohol consumers.

The fecal elastase-1 concentration test, 72-h fecal fat collection, and the $^{13}$C-mixed triacylglycerol breath test were used to diagnose pancreatic exocrine insufficiency [13]. Clinical pain scores were collected with the modified Brief Pain Inventory short form [25]. Using a 0-to-10 visual analog scale, pain severity was measured as the arithmetic mean of the current pain experience (i.e., pain right now) and the average, worst, and least pain during the previous 7 d. In addition, temporal pain pattern profiles were constructed on the basis of patients' reports of the worst, least, and average pain. Four distinct pain patterns were constructed as reported previously: no pain, intermittent pain, constant pain, and constant pain with acute exacerbations [3].

### *Statistical analysis*

All data are presented as mean ± SD unless otherwise indicated. The age, sex, and BMI distributions between patients with CP and controls were analyzed using Student's $t$ test and the $\chi^2$ test. The prevalence of underweight was reported as cohort proportions and compared using logistic regression with computation of the odds ratio and 95% confidence interval (CI). Differences in QOL scales and items were analyzed using Student's $t$ test or Wilcoxon's unpaired rank sum tests as appropriate. Putative associations between BMI and risk factors were analyzed using univariate regression analysis. Backward stepwise multivariate regression analysis was performed to evaluate independent predictors of low BMI. Variables that were significant on univariate analysis ($P < 0.1$) were included in multivariate modelling. Excessive collinearity was observed between pain-related parameters including pain severity scores, pain pattern, and opioid consumption. Consequently, three separate multivariate models were developed with inclusion of the three pain-related parameters separately and the additional parameters that were significantly associated with BMI on univariate analysis. The model performance of multivariate models was evaluated by the Akaike information criterion and Bayesian information criterion. All reported $P$-values were two-tailed, and values less than 0.05 were considered statistically significant. Data were analyzed using the software package STATA version 14.1 (StataCorp LP, College Station, TX, USA).

## Results

A total of 166 patients with CP and 160 controls were enrolled in the study. Baseline demographic and clinical characteristics are reported in Table 1. The median age was 58.6 y (23.5–84.9 y) in the CP group and 58.0 y (23.0–80.0 y) in the control group ($P = 0.24$). In the CP group, 70% of patients were male, compared with 69% in the control group ($P = 0.83$). The median Lünenburg score was 9 (4–23).

### *Body mass index and prevalence of underweight*

Patients with CP had decreased mean BMI compared with controls (22.9 ± 4.2 kg/m$^2$ versus 26.8 ± 5.2 kg/m$^2$; $P < 0.0001$). Distributions of BMI for patients with CP and controls are shown in Figure 1. Forty-three of 166 patients with CP (26.0% [95% CI: 19.8–33.1%]) were underweight compared with 15 of 160 controls (9.4% [95% CI: 5.8–14.9%]; odds ratio 3.38 [95% CI: 1.79–6.38]; $P = 0.0001$).

### *Underweight and life quality*

The European Organization for Research and Treatment of Cancer, Quality of Life Questionnaire-core 30 subscales and items stratified by nutritional state are reported in Table 2. A trend toward a decreased global health score was observed in underweight patients compared with patients with a normal BMI (39.9 ± 21.3 versus 49.6 ± 26.8; $P = 0.077$). Furthermore, underweight patients had decreased physical functioning compared with their normal-weight counterparts (52.3 ± 23.2 versus 64.7 ± 26.2) as well as a higher symptom level of pain ($P = 0.029$), appetite loss (0.039), and constipation ($P = 0.016$).

**Table 1**
Demographic and clinical characteristics of the study populations

| Patient characteristics | Patients with CP (n = 166) | Controls (n = 160) | *P*-value* | Complete data† |
|---|---|---|---|---|
| Demographic characteristics | | | | |
| Male, n (%) | 117 (70) | 111 (69) | 0.83 | 166 (100) |
| Age, y (IQR) | 58.6 (23.5–84.9) | 58.0 (23.0–80.0) | 0.24 | 166 (100) |
| Anthropometrics | | | | |
| Weight, kg | 67.1 ± 14.1 | 79.8 ± 1.4 | <0.001 | 166 (100) |
| Height, cm | 171.0 ± 8.6 | 172.5 ± 9.0 | 0.13 | 166 (100) |
| BMI, kg/m$^2$ (IQR) | 22.4 (19.7–25.0) | 26.2 (23.3–30.2) | <0.001 | 166 (100) |
| BMI category, n (%) | | | <0.001 | 166 (100) |
| <20 | 43 (26) | 15 (9) | | |
| 20–25 | 82 (49) | 43 (27) | | |
| 25–30 | 32 (19) | 59 (37) | | |
| >30 | 9 (5) | 43 (23) | | |
| CP characteristics | | | | |
| Etiology, n (%) | | | | 62 (98) |
| Alcoholic | 100 (62) | | | |
| Idiopathic | 39 (24) | | | |
| Other | 23 (14) | | | |
| Duration of CP, y (IQR) | 5.0 (2.0–11.0) | | | 163 (98) |
| Risk factors | | | | |
| Excessive alcohol consumption, n (%) | 13 (9) | | | 147 (89) |
| Smoking, n (%) | 102 (69) | | | 148 (89) |
| Pain | | | | |
| Pain severity, VAS (IQR) | 3.8 (1.6–5.4) | | | 132 (80) |
| Pain severity, n (%) | | | | 132 (80) |
| No pain | 23 (17) | | | |
| Mild pain | 34 (26) | | | |
| Moderate/severe pain | 75 (57) | | | |
| Pain pattern, n (%) | | | | 132 (80) |
| No pain | 23 (17) | | | |
| Intermittent pain | 9 (7) | | | |
| Constant pain | 100 (76) | | | |
| Opioid use, n (%) | 61 (43) | | | 142 (86) |
| EPI, n (%) | 128 (79) | | | 163 (98) |
| Diabetes, n (%) | 60 (36) | | | 165 (99) |
| QOL | | | | |
| Global health score | 47.5 ± 25.9 | | | 133 (80) |

BMI, body mass index; CP, chronic pancreatitis; EPI, exocrine pancreatic insufficiency; IQR, inter quartile range; QOL, quality of life; VAS, visual analogue scale
Percentages may not total 100 due to rounding
* Comparison of patients with CP and controls.
† Number (%) of patients with CP for whom complete data were available. All controls had complete data sets for the reported variables.

*Risk factors for underweight*

Univariate analysis identified seven factors that were potentially associated with BMI: duration of CP, alcoholic etiology, smoking, pain severity, pain pattern, opioid use, and EPI (Table 3, Fig. 2).

Alcoholic etiology (coefficient −2.39 kg/m$^2$; $P = 0.002$), EPI (coefficient −2.53 kg/m$^2$; $P = 0.004$), and constant pain (coefficient −1.82 kg/m$^2$; $P = 0.026$) were all significantly and independently associated with BMI in the most efficient multivariate model (Table 4). In the less efficient multivariate models, alcoholic etiology and EPI were significantly and independently associated with BMI, but a trend was observed for moderate/severe pain (coefficient −1.19 v; $P = 0.098$) and smoking (coefficient −1.44 kg/m$^2$; $P = 0.076$; Table 4).

## Discussion

We investigated the prevalence of underweight and its associated risk factors in a well-characterized cohort of outpatients with CP. One quarter of patients were underweight, which corresponds to a three-fold increased prevalence of underweight in patients with CP compared with age- and sex-matched controls. Underweight patients reported a reduced life quality and several modifiable risk factors that were associated with a low BMI, including alcoholic etiology, EPI, and pain-related symptoms. Our findings underline the necessity of a multidisciplinary approach in the handling of patients with CP, where a focus on alcohol cessation and appropriate treatment of pain and EPI should be prioritized.

*Prevalence of underweight*

Previous studies that investigated the prevalence of underweight and malnutrition in patients with CP reported highly variable estimates. This likely reflects differences in the definition used for classification and differences in the investigated patient cohorts [9–12]. In our study, 26% of patients were classified as underweight on the basis of a BMI cutoff of <20 kg/m$^2$. The BMI cutoff was chosen on the basis of recent published data from 10.6 million adults from the Global BMI Mortality Collaboration [18]. In this study, a substantially higher all-cause mortality rate was observed not only among those in the World Health Organization's underweight category (BMI <18.5 kg/m$^2$) but also in those with a BMI of 18.5 to 20 kg/m$^2$, which suggests that underweight is a cause for concern in excessively lean adults [18]. In patients with CP, an increased mortality rate also has been reported, and it is plausible that underweight may significantly contribute to mortality in addition to other parameters, including increased risk for malignancies and a high frequency of comorbidities [26].

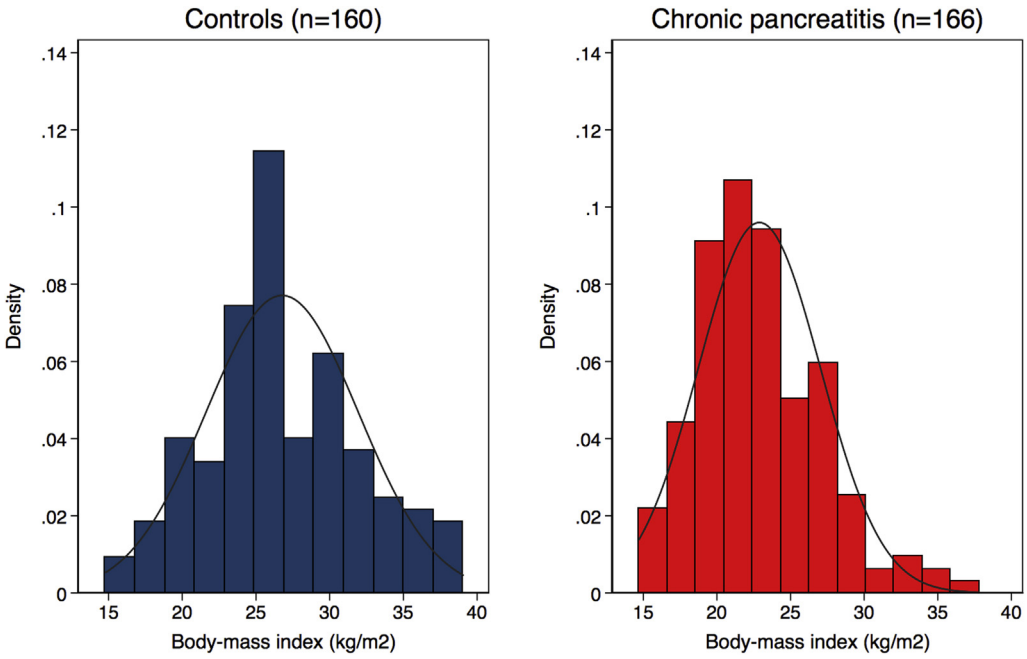


**Fig. 1.** Proportional distributions of body mass index in patients with chronic pancreatitis and healthy controls.

Using the definition of underweight that was recently commenced (BMI <20 kg/m$^2$), a multicenter study from Romania reported a prevalence of underweight patients who were admitted to a hospital with pancreatic disorders of 23% [12]. This was comparable with that observed in patients with gastrointestinal malignancies (26.8%) but significantly lower than that observed in patients with advanced liver disease (39.4%). However, the study did not provide details on the pancreatic diseases under investigation; as such, it was not clear whether patients with acute pancreatitis, pancreatic cystic lesions, or pancreatic malignancies were included in addition to patients with CP in the pancreatic disorder group [12].

In another study, Filipovic et al. observed a morbidly high prevalence of malnutrition (94%) in hospitalized patients with CP [9]. In this study, a subjective global assessment tool was used to characterize the nutritional status; once again, a direct comparison of the data with the prevalence estimate from our study is difficult because the authors did not provide detailed information on BMI [9]. Furthermore, it is likely that nutritional risk assessments tools are more sensitive than simple stratification by BMI, and this, in combination with the in-hospital setting, likely explains the much higher proportion of malnourished patients observed in the study by Filipovic el al. [6].

**Table 2**
EORTC QLQ-C30 subscales and items by BMI

| | Underweight (BMI <20 kg/m$^2$) | Normal weight (BMI ≥20 kg/m$^2$) | *P*-value |
|---|---|---|---|
| Global health | 39.9 ± 21.3 | 49.6 ± 26.8 | 0.077 |
| Functional scales | | | |
| Physical functioning | 52.3 ± 23.2 | 64.7 ± 26.2 | 0.024 |
| Role functioning | 45.7 ± 31.6 | 52.8 ± 35.3 | 0.34 |
| Emotional functioning | 55.4 ± 31.7 | 65.4 ± 30.1 | 0.094 |
| Cognitive functioning | 59.4 ± 26.1 | 67.4 ± 30.3 | 0.10 |
| Social functioning | 57.8 ± 31.5 | 66.0 ± 32.7 | 0.21 |
| Symptom scales/Items | | | |
| Fatigue | 63.4 ± 23.0 | 52.7 ± 30.9 | 0.11 |
| Nausea and vomiting | 23.7 ± 26.4 | 17.1 ± 23.6 | 0.20 |
| Pain | 67.7 ± 25.8 | 52.0 ± 34.3 | 0.029 |
| Dyspnea | 32.2 ± 32.1 | 26.7 ± 28.9 | 0.43 |
| Insomnia | 48.4 ± 30.8 | 46.8 ± 39.9 | 0.77 |
| Appetite loss | 52.7 ± 37.3 | 36.8 ± 39.6 | 0.039 |
| Constipation | 24.4 ± 28.9 | 13.9 ± 27.8 | 0.016 |
| Diarrhea | 22.2 ± 33.1 | 26.1 ± 30.7 | 0.91 |
| Financial difficulties | 49.4 ± 35.2 | 32.3 ± 39.7 | 0.023 |

BMI, body mass index; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer, Quality of Life Questionnaire-core 30

*Risk factors for underweight*

Several risk factors were associated with underweight in our study. As expected, EPI was strongly associated with underweight and resulted in a nearly 3-point drop in BMI if present. This is biologically plausible and in agreement with findings from numerous previous studies in which underweight and malnutrition have been consistently associated with EPI [13]. Importantly, enzyme replacement therapy significantly improves digestion; in most patients, when administered appropriately, enzyme replacement therapy largely restores digestion and improves patients' nutritional state [27]. In addition to EPI, an association between the duration of CP and BMI was observed in univariate analysis. However, this association was lost in the multivariate models and possibly reflects an interaction with one or more of the other parameters. Because EPI is known to develop as the fibroinflammatory process that underlies CP evolves, it is plausible that the association between EPI and duration of CP that was observed in univariate analysis indirectly reflected the development of EPI [15].

An important finding of our study was the strong association between pain-related symptoms (pain severity, pain pattern, and opioid treatment) and BMI. Many patients with CP experience pain, and pain severity, pain pattern in time (i.e., intermittent versus constant pain), and opioid treatment have previously been associated with a decreased QOL and increased health resource utilization [3,4,23]. Nonetheless, to our knowledge, a direct relationship between underweight and pain symptom burden has not previously been established in the context of CP.

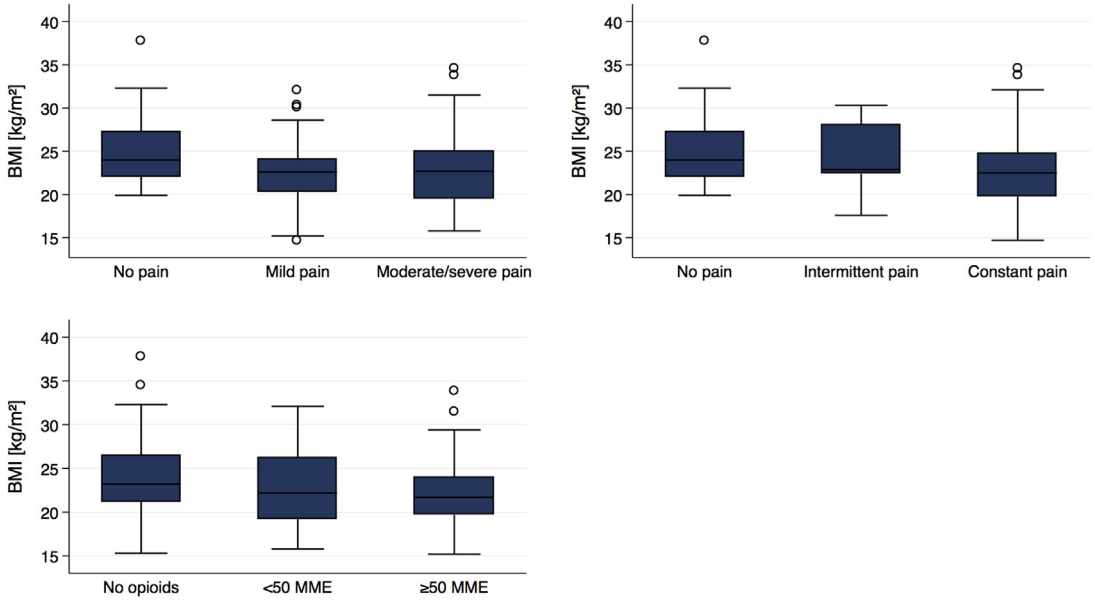


**Fig. 2.** Body mass index in patients with chronic pancreatitis stratified by pain severity, pain pattern in time, and opioid-based treatment.

Our findings are clinically meaningful because patients with severe and constant pain are likely to reduce their calorie intake due to anorexia and a fear of meal-induced pain provocation [28]. Furthermore, opioid-based treatments may induce nausea and loss of appetite, which further compromise nutritional intake. Also, opioid treatment is associated with a range of other gastrointestinal side effects that are commonly referred to as opioid-induced bowel syndrome, which may compromise nutritional intake further [29]. Taken together, pain-related symptoms and opioid treatment place the patient at risk of underweight and malnutrition; therefore, optimal and preferably non–opioid-based pain treatments should be a priority in all patients with CP, not only to reduce troublesome pain symptoms but also to improve nutritional status and disease outcome.

Smoking and an alcoholic etiology of CP were associated with BMI in univariate analyses. Alcohol is a well-established risk factor for CP, and some data indicate that patients with alcoholic CP have an accelerated development of exocrine and endocrine insufficiency and more pain compared with patients with an idiopathic etiology [15]. As such, unsurprisingly, alcoholic etiology was associated with a low BMI. We were not able to establish an association between ongoing excessive alcohol consumption and low BMI, which may be explained by the relative small number of patients in the excessive alcohol consumer group, introducing the risk of type-2 error. Furthermore, the validity of self-reported drinking habits may be questioned but unfortunately, we did not include any objective markers of ongoing alcohol abuse. Therefore, some patients may have been misclassified with regard to alcohol consumption and a lack of association between BMI and excessive alcohol consumption should be interpreted with caution. As such, alcohol abstinence remains a priority in the handling of patients with CP.

**Table 3**
Univariate analysis of putative risk factors associated with decreased body mass index in outpatients with chronic pancreatitis

| | Coefficient (95% Confidence Interval)* | *P*-value |
|---|---|---|
| Age† | 0.04 (−0.52 to 0.59) | 0.90 |
| Male sex | 1.10 (−0.30 to 2.50) | 0.12 |
| Duration of CP† | −0.77 (−1.63 to 0.10) | 0.08 |
| Alcoholic etiology | −2.24 (−3.53 to −0.94) | 0.001 |
| Excessive alcohol consumption | −1.08 (−3.47 to 1.32) | 0.38 |
| Smoking | −2.45 (−3.90 to −1.00) | 0.001 |
| Pain severity | | |
| No pain | Reference | |
| Mild pain | −2.29 (−4.46 to −0.11) | 0.04 |
| Moderate/severe pain | −2.23 (−4.15 to −0.32) | 0.02 |
| Pain pattern | | |
| No pain | Reference | |
| Intermittent pain | −1.06 (−4.22 to 2.09) | 0.51 |
| Constant pain | −2.36 (−4.21 to −0.50) | 0.01 |
| Opioid use | −1.42 (−2.78 to −0.05) | 0.04 |
| EPI | −2.86 (−4.38 to −1.35) | <0.001 |
| Diabetes | 0.63 (−0.70 to 1.96) | 0.35 |

CP, chronic pancreatitis; EPI, exocrine pancreatic insufficiency
* 95% confidence intervals were calculated using bootstrap-corrected analysis.
† The coefficients are based on changes of 10 y for age and duration of CP.

During the last decade, smoking has been established as a significant and independent risk factor for patients with CP [30–32], and a recent study linked the fibroinflammatory process that underlies CP with smoking through an interleukin 22–mediated pathway, thus providing a mechanistic explanation [33]. A strong association between BMI and active smoking was observed in univariate analysis, but this association was lost in multivariate analyses, possibly implying that the contribution of smoking to underweight in patients with CP is complex and interacts with other parameters, including EPI and alcoholism. Nonetheless, patients should be advised to quit smoking when a diagnosis of CP is established because smoking cessation may decelerate the evolution of exocrine and endocrine insufficiency and thus improve outcome [34].

### *Study strengths and limitations*

This study was undertaken in a large population of well-characterized patients with CP. To our knowledge, this is the largest study to examine the prevalence of underweight and its associated risk factors in this context. The large sample size allowed for detailed stratification and analysis of putative risk factors. Additionally, the age- and sex-matched control group

**Table 4**
Multivariate analysis of risk factors associated with decreased body mass index in outpatients with chronic pancreatitis

| Variables introduced | Final model | Coefficient (95% Confidence Interval) | *P*-value | AIC | BIC |
|---|---|---|---|---|---|
| Alcoholic etiology, duration of CP, smoking, EPI, Pain severity | Alcoholic etiology | −2.40 (−3.89 to −0.92) | 0.002 | 663.8 | 674.9 |
| | EPI | −2.68 (−4.40 to −0.95) | 0.003 | | |
| | Moderate/severe pain | −1.19 (−2.62 to 0.22) | 0.098 | | |
| Alcoholic etiology, duration of CP, smoking, EPI, Pain pattern | Alcoholic etiology | −2.39 (−3.86 to −0.93) | 0.002 | 661.5 | 672.6 |
| | EPI | −2.53 (−4.24 to −0.82) | 0.004 | | |
| | Constant pain | −1.82 (−3.41 to −0.23) | 0.026 | | |
| Alcoholic etiology, duration of CP, smoking, EPI, Opioid treatment | Alcoholic etiology | −1.85 (−3.37 to −0.34) | 0.017 | 691.1 | 702.4 |
| | EPI | −2.87 (−4.61 to −1.12) | 0.001 | | |
| | Smoking | −1.44 (−3.04 to 0.15) | 0.076 | | |

AIC, Akaike information criterion; BIC, Bayesian information criterion; CP, chronic pancreatitis; EPI, exocrine pancreatic insufficiency

allowed us to compare the risk of underweight with that observed in a healthy population.

Some limitations of the present study should be recognized. First, the cross-sectional nature of our study precludes definitive causal inferences about the relationship between underweight and the reported risk factors. However, plausible biological mechanisms exist for all the identified risk factors, and a large body of evidence from basic and clinical studies supports their relevance in the context of CP. Second, data regarding previous and current alcohol consumption and comorbidities, as well as detailed stratification of tobacco use and medication, were not available for this study. Prospective longitudinal studies including objective markers of excessive alcohol consumption are needed to minimize recall bias and misreporting from patients. Finally, BMI is a very simple proxy for patients' overall nutritional state, and future studies should focus on a more accurate and detailed characterization on the basis of validated nutritional assessment tools, preferably combined with objective methods such as electrical bioimpedance, dual-energy x-ray absorptiometry, or cross-sectional imaging with quantification of muscle and fat mass.

## Conclusions

One quarter of outpatients with CP are underweight and report a reduced QOL compared with their normal-weight counterparts. Alcoholic etiology, EPI, and pain-related symptoms are significant and independent risk factors for underweight. These findings emphasize the need for a multidisciplinary approach in the handling of patients with CP, where focus on alcohol abstinence and appropriate treatment of pain and EPI should be prioritized.

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