Applied nutritional investigation

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

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 $\pm$ 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 χ^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 $\pm$ 4.2 kg/m^2 versus 26.8 $\pm$ 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 $\pm$ 21.3 versus 49.6 $\pm$ 26.8; $P = 0.077$). Furthermore, underweight patients had decreased physical functioning compared with their normal-weight counterparts (52.3 $\pm$ 23.2 versus 64.7 $\pm$ 26.2) as well as a higher symptom level of pain ($P = 0.029$), appetite loss (0.039), and constipation ($P = 0.016$).