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Original Article

A population-based study of chronic pancreatitis in Finland: Effects on quality of life

Mikael Parhiala [a], Juhani Sand [b], Johanna Laukkarinen [a, b, *]

[a] Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland
[b] Dept of Gastroenterology and Alimentary Tract Surgery, Tampere University Hospital, Tampere, Finland

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ABSTRACT

Background/Objectives: In Finland the incidence of chronic pancreatitis (CP) is high compared to that in most European countries. Recent epidemiological data is lacking. Our aim was to investigate the current epidemiologic and behavioural data on CP patients in Finland.
Methods: CP patients according to M-ANNHEIM criteria in Tampere University Hospital (TAUH) during 2014–2015 were included. Aetiology, time from diagnosis, pancreatic function, treatment, complications, smoking, alcohol consumption (AUDIT) and quality of life (QoL) (QLQ C30, PAN26) were gathered.
Results: 235 CP patients (57 (26–88) years, 65% men) were included. Time since diagnosis was 5.5 (1–41) years. Aetiology was alcohol in 67%, and smoking contributed in 54%. Of these patients 78% continued smoking and 58% continued to consume alcohol even after CP diagnosis. CP related complications were common. Pseudocysts were more common in alcohol related CP than in non-alcohol related CP (60% vs. 38%, $p < 0.05$). Reported QoL and pain were worse in the CP patients than in controls. Alcohol consumption differed from that of the Finnish population; the CP patients were either total abstainers or heavy alcohol consumers.
Conclusions: CP constitutes a great burden on the health care system and on the patients. The patients frequently develop complications and symptoms and their QoL is inferior to that of controls. The most important measure to halt the progression of CP would be to prevent acute phases and for patients to stop smoking, which does not happen in many CP patients. It would be beneficial to increase awareness among CP patients and medical professionals.

Introduction

Chronic pancreatitis (CP) causes permanent morphological changes to the pancreatic tissue. The persistent inflammation may lead to abdominal pain and pancreatic insufficiency, seen as secondary diabetes and malnutrition, as well as to various complications such as pseudocysts [1–4]. Furthermore, CP patients carry a slightly increased risk for pancreatic cancer, especially those suffering from pancreatitis at a young age due to prolonged inflammation, which constitutes a risk factor [5–7]. Out of the multiple CP aetiologies, the most recognized and common is alcohol, which causes about 70% of the CP in Western countries. Other risk factors for CP include duct obstruction, hyperlipidaemia, autoimmune, hereditary and anatomical factors [8,9]. The most prominent symptom of CP is persistent or recurring abdominal pain. Treatment of CP pain is not easy, and strong opioids may be needed. The progression of CP can be delayed by stopping smoking and preventing acute phases. Smoking exacerbates CP but is not the sole cause. Avoiding alcohol and smoking would thus be crucial in the prevention of disease progression [10].

In Western countries the prevalence of CP is between 43 and 143/100,000 in Europe and 41–91/100,000 in the USA [2,11–14]. In Finland the incidence of acute pancreatitis (AP) is 70/100,000 and the incidence of CP 13.4/100,000, which is one of the highest incidences of CP in Europe. However, no recent epidemiological data involving CP in Finland exists [15,16].

Objectives

The aim of this study was to investigate the current status and treatment of CP in Finland; findings, complications, pancreatic function, conservative and interventional treatment, lifestyle habits and quality of life (QoL).

* Corresponding author. Dept. of Gastroenterology and Alimentary Tract Surgery, Tampere University Hospital, Teiskontie 35, FIN-33521, Tampere, Finland.
E-mail address: johanna.laukkarinen@fimnet.fi (J. Laukkarinen).

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Methods

All adult patients who had been treated for CP (ICD-10 diagnosis code K86*) in Tampere University Hospital (TAUH) in the period 2014–2015 were selected and reviewed for inclusion in the database.

The diagnostic criteria according to M-ANNHEIM were used. This classification system for CP considers multiple risk factors: alcohol, nicotine, nutrition, hereditary factors, efferent duct factors, immunological factors and miscellaneous factors. In our study we grouped all the unknown aetiologies into miscellaneous factors. The M-ANNHEIM diagnostic criteria are grouped into definitive and probable. The definitive criteria involve one or more of the following: pancreatic calcifications, moderate or marked ductal lesions (according to the Cambridge classification), exocrine insufficiency requiring pancreatic enzyme supplementation or an adequate histological specimen. The probable criteria include mild duct lesions, persistent/recurrent pseudocysts, pathological test of exocrine or endocrine function of the pancreas i.e. low faecal elastase or abnormal glucose tolerance. The diagnosis also requires a typical clinical history of CP which includes recurrent abdominal pain or pancreatitis, except for painless pancreatitis [10].

Medical records of all patients were reviewed. Patients who did not meet the diagnostic criteria were excluded from the database. The patients who were verified as CP patients formed the final database. The following data was collected: date of birth, gender, pancreatic insufficiency, aetiologies, complications, year of diagnosis, mortality, alcohol consumption, smoking, interventions and imaging findings. Originally 235 patients were identified. After excluding the patients who were deceased or whose address information was not available, 188 patients were asked to complete the QoL questionnaires EORTC (European Organisation for Research and Treatment of Cancer) QLQ-C30 and pancreatic specific EORTC QLQ-PAN26 [18]. Mortality was recorded on November 4, 2018. The follow-up time median from the beginning of the disease was five years (2–43 years).

A Swedish control population (n = 3069; mean age 51 years, 53% female) was used as a control population for the QLQ-C30 [19]. Sweden and Finland have similar lifestyles and climate, both of them being Nordic countries. In the C30 normative population 5% of subjects had suffered from asthma, while in the Finnish population 4–7% had asthma, 5% of the C30 had diabetes while 5–6% of the Finnish population had diabetes [20].

A normative control from the UK was used for the PAN26 questionnaire responses [21], the normative population includes n = 101 responders, median age 39.5 (range 20–84) years. The Finnish AUDIT (Alcohol Use Disorders Identification Test) control population (n = 1,368, 44% male 28–79 years) was used as a control population for alcohol consumption; Mäkelä Pia 2017 Finnish Drinking Survey THL [22].

Data is presented as medians (range) unless otherwise stated. The statistical analysis was calculated by IBM SPSS statistic version 24 using Pearson's Chi-Square or Fisher's exact test, for the analysis of the QLQ-C30 and PAN26 questionnaires the Mann-Whitney U -test was used. The EORTEC scoring manual was used for the QLQ-C30 and PAN26 questionnaires, the responses were scored to 0–100. A higher score in QOL/functioning represents a better score and a lower score in symptoms (e.g. pain or insomnia) represents a better score. $P < 0.05$ was considered statistically significant.

Ethical aspects

The study was approved by the Ethics committee of Tampere University Hospital, Finland (ETL code R15187).

Results

In total 235 CP patients who met the CP diagnostic criteria were included in the final study database. Median age was 57 years (26–88 years), and 65% were male. The median time since diagnosis was 5.5 (1–41) years. Of the CP patients 91% (n = 216) met one or more of the definitive diagnostic criteria for CP. Recurrent AP was recorded in sixty-four percent. Out of the 235 patients, 219 underwent radiological imaging during the follow-up period: 37% had marked changes, 20% had moderate changes, 12% had mild changes, 19% had equivocal changes and 12% had normal pancreas during imaging.

The aetiology was diverse and multiple aetiologies were common (Table 1). Alcohol consumption combined with smoking was the leading factor for CP; 50% of the patients reported at least alcohol consumption and smoking as risk factors. We have information about smoking history on 234/235 patients (99.6%) and about alcohol consumption on 232/235 patients (98.7%), but without information on the amount of alcohol consumed. Smoking was a risk factor in 54% and 78% continued smoking after their diagnosis. Smoking pack-years (20 cigarettes per day for a year) median was 37 years (5–70 years) n = 66 (52% all smokers). A further 20% had unknown aetiologies for CP and 10% had efferent duct factors as a risk factor. Six patients underwent genetic testing and five patients were found to have a SPINK1 mutation.

Twenty-six percent of the patients (n = 60) died during follow-up at a median age of 62 (range 26–85). Females died at a median age of 63 years and males 62 years. Cause of death was available for 21 patients, and these are listed in Table 1. In the year 2017 the median age of death in Finland was 75 years for men and 81 years for women.

Complications are listed in Table 1. Pancreatic calcifications were found in 66% of patients and ductal lesions in 50%. Of the patients 55% had pancreatic exocrine insufficiency (PEI) and 54% had pancreatic endocrine insufficiency (High HbA1c count or fasting blood sugar levels diagnostic for diabetes mellitus). Pseudocysts were more common in alcohol related CP than in non-alcohol related CP (60% vs. 38%, p = 0.0005). In patients who smoked, pseudocysts (62% vs. 52% p = 0.262; ns) and pancreatic calcifications tended to be slightly more frequent (72% vs. 58% P = 0.071; ns) than among non-smokers. Bile duct stenosis requiring interventions was found in 10% and 7% of the patients had abdominal ascites and pleural effusion, and a further 5% of the patients with CP also had liver cirrhosis.

Interventions are listed in Table 1. Endoscopic procedures where performed on 27% of the patients. Out of these, 20% needed endoscopic interventions multiple times and one patient had an endoscopic celiac blockage.

Nine per cent of the patients underwent surgical procedures. Surgical interventions (n = 21) included treatments for complications, such as pseudocysts or stenosis, involving cystojejunostomies (n = 11), gastrojejunostomies (n = 2) and hepaticojejunostomies (n = 2). Whipple procedures (n = 4) were mostly performed to rule out malignancies. Two Beger-type operations were performed.

Out of the 188 patients requested to complete the questionnaires, 77 (41%) returned the QoL questionnaires (QLQ-C30 and Pan-26) and 76 (40%) the AUDIT questionnaire (Fig. 1). Among the responders who answered the questionnaires the median age was 57 years (range 28–88), the median since diagnosis was four years (range 2–42 years). The proportion of alcohol aetiologies, pseudocysts and PEI were similar compared to all patients alive in the total study population. Out of 77 patients who responded six died in 2-year follow-up. Patients who died had statistically higher pancreatic pain (49 vs. 29) p = 0.042, financial difficulties, difficulties in physical functioning and in cognitive functioning.

Table 1
a) Demographics, risk factors and complications of CP patients in a Finnish tertiary hospital in 2014–2015. b) Complications by risk factors c) Multiple risk factors are possible. Alcohol and smoking are the largest risk factors of CP in Finland. Efferent duct factors include mostly bile duct stones. Immunological factors include autoimmune pancreatitis and Sjögren's syndrome. All of the Hereditary CP was connected to SPINK1 mutation.

a

Chronic pancreatitis patients n = 235	
Age median	58 *(26–95) years*
BMI median (n = 109)	23 [16–48]
Gender	34% female 67% male
Time after diagnosis median (range) n = 107	4 [1–42] *years*
Risk factors n = 234	
Alcohol	68%
Nicotine	54%
Unknown	21%
Efferent duct factors	10%
Hereditary	3%
Immunological	3%
Nutrition	2%
More than one aetiology	57%
One aetiology	43%
Smoking pack years median (range) n = 66	37 (5–70) years
Complications n = 234	
Calcifications	66%
Pseudocysts	58%
Exocrine insufficiency	55%
Endocrine insufficiency	54%
Ductal lesions	50%
Bile duct stenosis	10%
Pleural effusion	7%
Ascites	7%
GI-tract bleeding	6%
Pancreatic fistulas	5%
Porta thrombosis	5%
Pseudoaneurysms	5%
GI-tract stenosis	4%
Death	(n = 60) 26%
Cause of death in CP n = 21 (35%)	
Cardiovascular disease	19%
Other malignancy	19%
Liver cirrhosis	14%
COPD (Chronic Obstructive Pulmonary Disease)	10%
Hypoglycemia	10%
Pancreatitis	10%
Pancreatic adeno ca	5%
Polycystic kidney disease	5%
Sepsis	5%
Post surgery sepsis	5%
Interventions n = 234	34%
Endoscopic	27%
Surgery	9%
Percutanous drainage	8%
Celiac block	0.40%

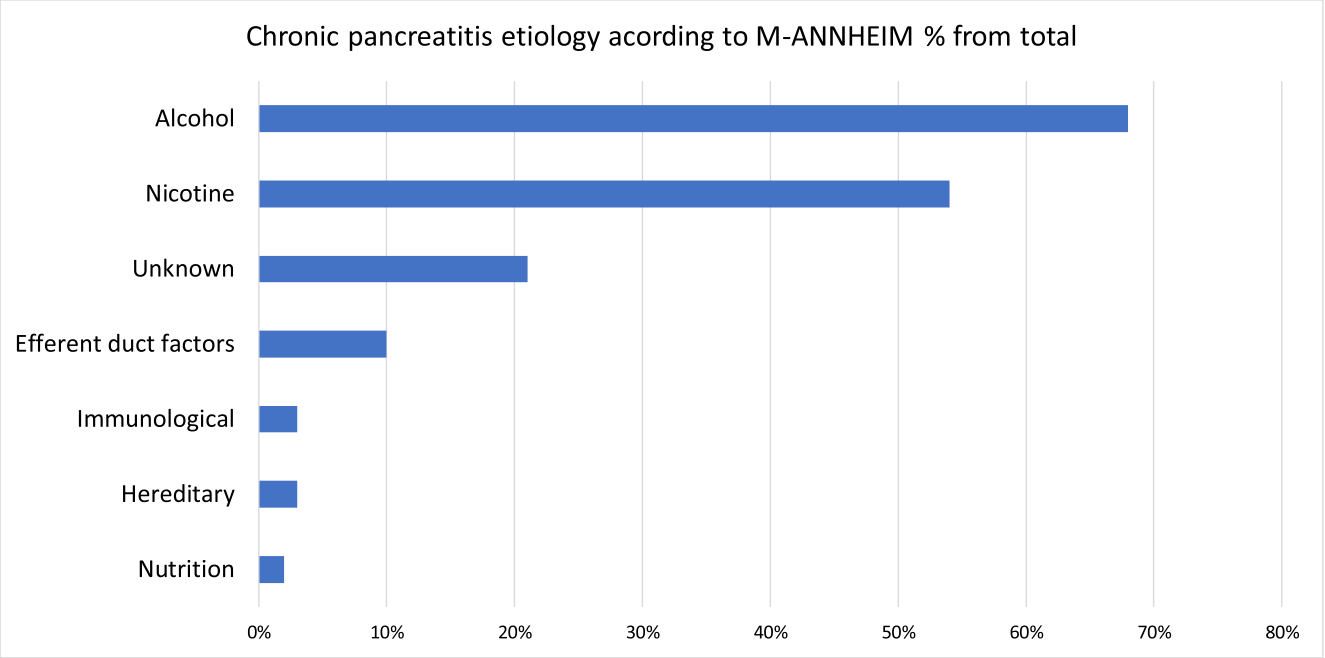
b

Risk factors and complications		Calcifications		Pseudocysts		Any complication	
Alcohol n = 232	**Yes**	74%	p«0.05	66%	p«0.05	72%	p«0.05
	No	50%		42%		46%	
Smoking n = 234	**Yes**	65%	p = 0.071	61%	P = 0,262	68%	p = 0.103
	No	53%		54%		58%	

c

Table 1 (*continued*)

c



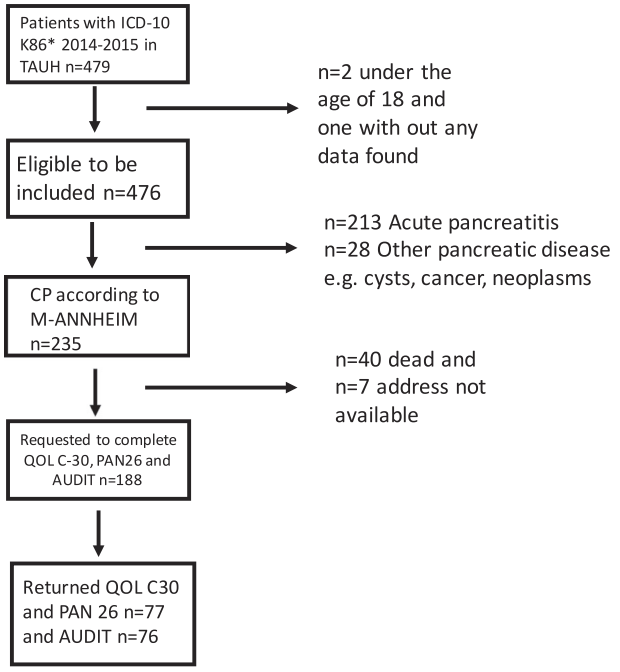
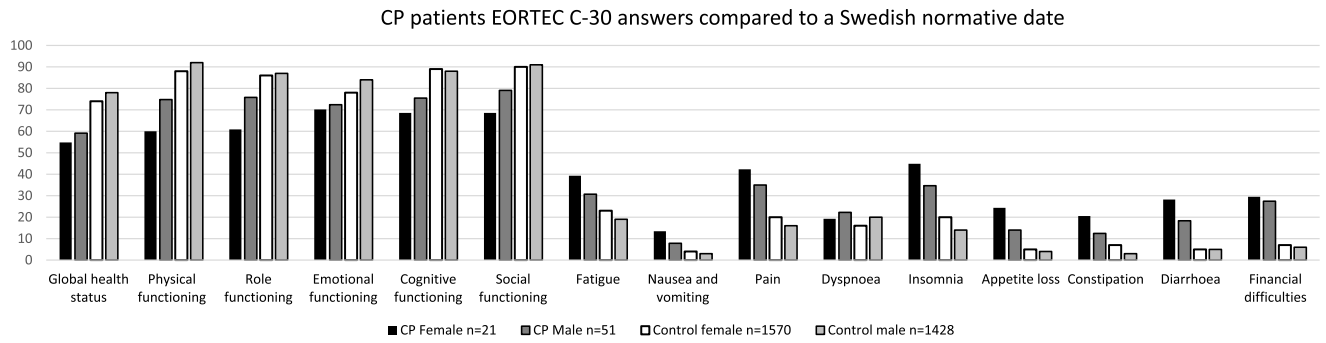


Fig. 1. Flowchart of CP patient recruitment in TAUH 2014–2015.

The QLQ-C30 and Pan26 data (n = 77) are shown in Figs. 2 and 3. There was no statistically significant difference in the C30 and PAN26 in men and female CP patients except for men having better physical functioning and fewer digestive symptoms. In the C30 responses all functioning, and symptoms were poorer in CP patients than in the controls. In the PAN26 all symptoms were statistically more severe than in the control group but for satisfaction with health care no difference was found.

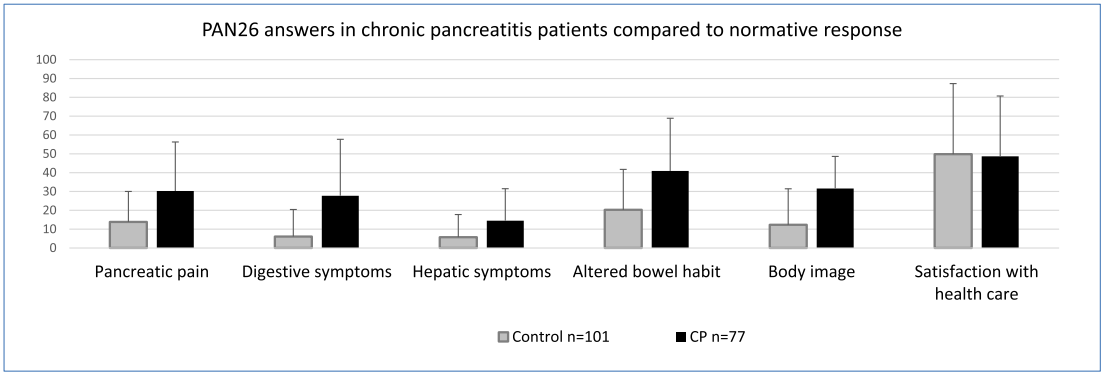
When comparing the EORTC QLQ C30 and PAN26 questionnaire responses between smoking and non-smoking patients, smokers had poorer functioning and more severe symptoms in all categories, although not all of the categories reached statistical difference. For example, there was a statistical difference in pain and pancreatic pain. (Fig. 4). This difference was not found when comparing AUDIT (0 points, 6 Female/8 male or 16 or over points) scores to responses on pain or pancreatic pain. (Fig. 5). There was no significant difference in pain or pancreatic pain in any of the groups. No significant differences in the pancreatic-specific responses (PAN26) were found when grouping the AUDIT questionnaires except for hepatic symptoms when comparing AUDIT<16p vs AUDIT ≥16p (12 vs 26 mean; p = 0.018). There were many statistical differences between the C30 responses to different AUDIT scores (Fig. 5).

Fig. 6a shows the distribution of AUDIT scores compared to those of 28 to 79-year-old Finnish men and women. The AUDIT scores were grouped into four groups, the first group being 0–6 points for women and 0–8 points for men based on the Finnish Current Care Guidelines screening limits for hazardous alcohol consumption. CP patients more often scored over 16 points on AUDIT than did the rest of the population (16% vs. 3%; p < 0.005). In addition, CP patients more often scored over six for females and over eight for males, compared to the controls (33% vs 23%; p = 0.041). Total abstinence among the CP patients was 42%, and women had a higher percentage of total abstinence (62% vs. 32%; p = 0.013). Since abstinence differed greatly by age and gender, we divided it into two age groups per gender (Fig. 6b). In males aged 28–59 years abstinence was 26% in CP patients vs. 10% in controls; p = 0.006. In women aged 28–59 years abstinence was 50% in CP patients vs. 13% in controls; p = 0.0001). CP men over 60 years (42% vs. 14%; p = 0.001) and women over 60 years (75% vs. 26%; p = 0.0002) were more often total abstainers from alcohol than were the controls.



EORTEC QLQ-C30 data from chronic pancreatitis patients Functioning and quality of life	n=77 CP	(st dev)	n=26 CP female	n=51 CP male	p-value Female vs male	*n=1570* *Control female***	*n=1428* *Control male***	n=35 Non-smoking (st dev)	n=42 Smoking (st dev)	p-value Smoking vs non-smoking
Higher the value= better functioning										
QOL	58	(24)	55 (26)	59 (23)	0.54	*74 (22)*	*78 (21)*	63 (21)	54 (25)	0.065
Physical functioning	70	(26)	60 (26)	75 (24)	**0.017***	*88 (18)*	*92 (16)*	75 (22)	65 (28)	0.142
Role functioning	71	(31)	61 (35)	76 (28)	0.076	*86 (24)*	*87 (24)*	77 (26)	66 (34)	0.313
Emotional functioning	72	(28)	70 (28)	72 (27)	0.651	*78 (22)*	*84 (20)*	84 (20)	62 (29)	**0.001***
Cognitive functioning	73	(28)	69 (34)	75 (23)	0.746	*89 (18)*	*88 (17)*	87 (15)	62 (31)	**0.000***
Social functioning	76	(34)	69 (34)	79 (34)	0.097	*90 (20)*	*91 (19)*	81 (34)	71 (34)	**0.0138**
Symptoms: Higher the value= worse symptoms										
Fatigue	34	(27)	39 (29)	31 (26)	0.208	*23 (22)*	*19 (21)*	21 (19)	44 (29)	**0.000***
Nausea and vomiting	10	(18)	13 (24)	8 (15)	0.39	*4(11)*	*3 (10)*	3 (8)	15 (23)	**0.005***
Pain	37	(32)	42 (35)	35 (30)	0.469	*20(27)*	*16 (23)*	29 (29)	44 (33)	**0.035***
Dyspnoea	21	(29)	19 (34)	22 (25)	0.197	*16 (24)*	*20 (28)*	13 (22)	28 (32)	**0.041***
Insomnia	38	(35)	45 (37)	35 (33)	0.256	*20 (28)*	*14 (25)*	30 (29)	44 (38)	0.118
Apetita loss	18	(26)	24 (30)	14 (23)	0.112	*5 (15)*	*4 (14)*	8 (16)	26 (30)	**0.002***
Constipation	15	(24)	21 (29)	12 (20)	0.287	*7 (18)*	*3 (12)*	10 (20)	20 (25)	**0.035***
Diarrhoea	22	(27)	28 (37)	18 (20)	0.599	*5 (16)*	*5 (15)*	15 (23)	27 (29)	0.056
Financial difficulties	28	(36)	29 (38)	27 (35)	0.986	*7 (21)*	*6 (19)*	10 (26)	43 (37)	**0.000***

Fig. 2. Quality of life: overall. QLQ-C30 scores (mean, SD) in CP patients compared to the Swedish normative data (15). All functioning and symptom scores are worse in CP patients compared to the controls. The smoking CP group had worse functioning and symptoms scores. A higher score in QOL/functioning represents a better QoL. A lower score in symptoms represents a better QoL.



QLQ-PAN26 data from chronic pancreatitis patients	n=77 kpl CP (st dev)	n=26 CP female	n=51 CP male	p-value Female vs male	n=101 Control population**	n=35 Non-smoking (st dev)	n=42 Smoking (st dev)	p-value Smoking vs non-smoking
Pancreatic pain	30 (26)	38 (30)	26 (23)	0.088	14 (16)	22 (23)	37 (27)	**0.007***
Digestive symptoms	28 (30)	40 (31)	21 (27)	**0.005***	6 (14)	21 (24)	33 (33)	0.157
Altered bowel habit	41 (28)	47 (30)	38 (27)	0.281	20 (21)	32 (23)	48 (30)	**0.015***
Hepatic symptoms	15 (17)	16 (20)	14 (16)	0.811	6 (12)	9 (14)	19 (18)	**0.005***
Body image	32 (30)	40 (38)	27 (25)	0.316	13 (19)	20 (20)	41 (34)	**0.005***
Satisfaction with health care	49 (32)	40 (36)	53 (29)	0.086	50 (37)	52 (32)	46 (32)	0.411
***Swedish population (Michelson et al.2000)*				**Statistically significant***				

Fig. 3. Quality of life: overall. QLQ-PAN26 scores (mean, SD) in CP patients compared to a normative Chicago population (17). All symptoms are worse compared to the control. A lower score in symptoms represents a better score, except for satisfaction with health care. CP patients have worse scores in all parameters except satisfaction with health care. CP that smoke had worse pancreatic pain, altered bowel habits, hepatic symptoms and body image.

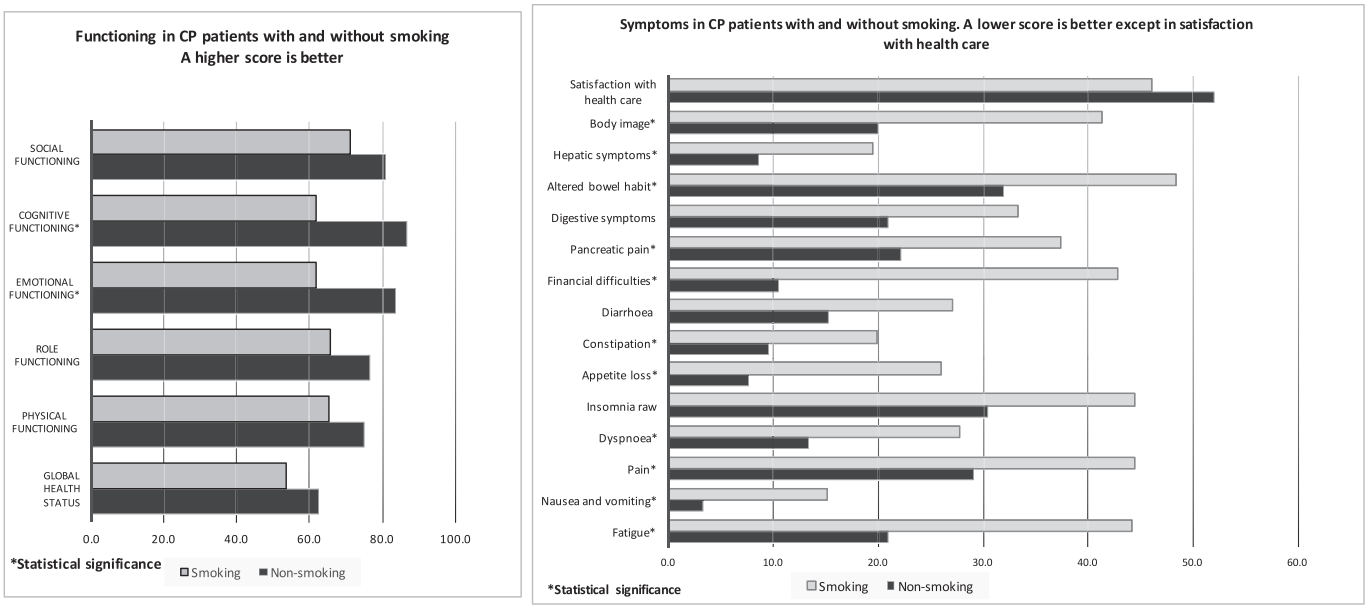


Fig. 4. Quality of life: smoking. QLQ C30 and PAN26 functioning and symptom scores in CP patients who smoke and do not smoke. CP patients who smoke have worse functioning QoL and more symptoms. * marks as a statistical significance ($p < 0.05$). A lower score in symptoms represents a better QoL, except for financial difficulties.

AUDIT scores compared to EORTEC QLQ-C30 and PAN26 data									
Functioning and quality of life	**n=46**	**n=31**		**n=51**	**n=26**		**n=64**	**n=13**	
Higher the value= better functioning	*AUDIT=0p*	*AUDIT ≥ 1p*	*p-value*	AUDIT≤ 6F/8M	AUDIT > 6F/8M	p-value	AUDIT < 16 points	AUDIT≥1 6 points	p-value
QOL	*61.2*	*55.2*	*0.286*	62.8	48.1	**0,026***	60.8	42.3	**0.018***
Physical functioning	*72.1*	*68.1*	*0.724*	71.1	66.9	0.696	70.5	66.2	0.666
Role functioning	*72.4*	*69.6*	*0.991*	74.0	64.7	0.498	72.1	64.1	0.628
Emotional functioning	*78.6*	*66.7*	*0.135*	78.2	59.3	**0.028***	76.3	48.7	**0.008***
Cognitive functioning	*80.7*	*67.8*	*0.052*	78.7	62.2	**0.018***	77.9	50.0	**0.001***
Social functioning	*26.7*	*38.5*	*0.291*	27.6	46.2	0.124	29.7	53.0	**0.046***
Symptoms: Higher the value= worse symptoms									
Fatigue	*4.2*	*13.7*	*0.152*	5.3	18.6	**0.009***	6.0	28.2	**0.008***
Nausea and vomiting	*31.8*	*41.5*	***0.007****	32.7	46.2	**0.002***	34.4	52.6	**0.000***
Pain	*14.6*	*26.5*	*0.195*	17.0	29.5	0.199	17.7	38.5	0.124
Dyspnoea	*30.2*	*43.7*	*0.062*	30.0	53.8	0.094	31.8	69.2	**0.014***
Insomnia	*12.5*	*21.2*	*0.126*	12.0	29.3	**0.005***	12.5	44.4	**0.001***
Apetita loss	*13.5*	*16.3*	*0.191*	13.3	19.2	**0.003***	13.5	23.1	**0.000***
Constipation	*14.6*	*26.7*	*0.547*	14.0	35.9	0.149		38.5	0.050
Diarrhoea	*21.9*	*32.6*	***0.038****	22.7	39.7	**0.000***	24.5	46.2	**0.005***
Financial difficulties	*26.8*	*33.0*	*0.199*	26.8	37.8	**0.037***	28.6	39.1	**0.045***
QLQ-PAN26 data from chronic pancreatitis patients									
Pancreatic pain	*26.8*	*33.0*	*0.463*	26.8	37.8	0.204	28.6	39.1	0.366
Digestive symptoms	*27.6*	*27.8*	*0.663*	25.7	32.7	0.530	27.6	28.2	0.656
Altered bowel habit	*34.9*	*45.2*	*0.180*	37.3	48.1	0.214	39.8	46.2	0.673
Hepatic symptoms	*10.9*	*17.0*	*0.192*	11.7	19.2	0.111	12.2	25.6	**0.018***
Body image	*25.5*	*35.9*	*0.214*	27.0	41.0	0.060	29.4	42.3	0.135
Satisfaction with health care	*55.7*	*43.6*	*0.129*	52.4	41.7	0.184	51.3	35.9	0.109
*Statistically significant									

Fig. 5. Quality of life: AUDIT scores. And CP patients with a higher AUDIT score had worse functioning and symptoms in the QLQ-C30 responses but there was no difference in the PAN26 responses except for hepatic symptoms when comparing AUDIT plus 16 points. A higher score in functioning represents a better score. A lower score in symptoms represents a better score, except for satisfaction with health care.

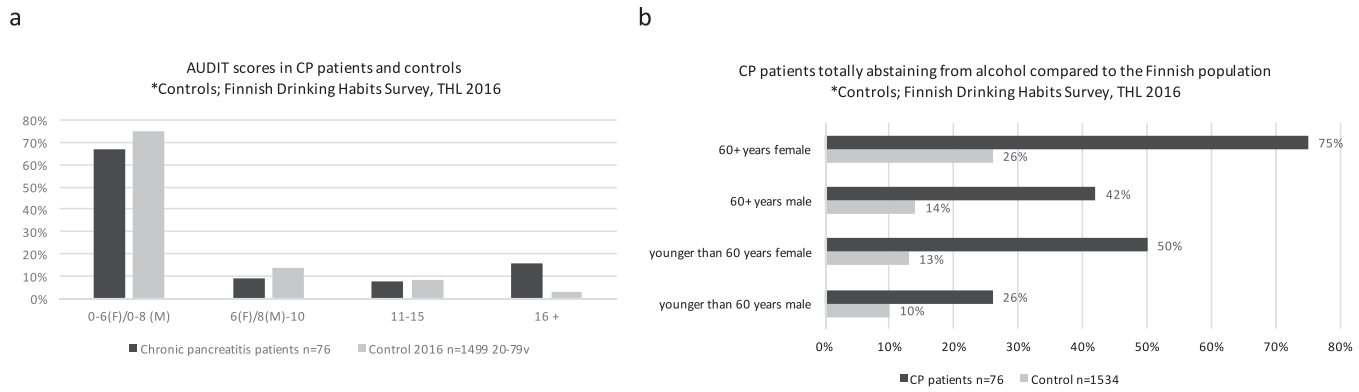


Fig. 6. Alcohol usage. a) AUDIT score distribution in CP patients n = 76 compared to the Finnish population (18) of the same age. Male and female scores were grouped differently due to different scores ratings. There was a statistical difference between 0 and 6 (Female)/0–8 (male) groups and 16+ groups ($p < 0.05$). b) The distribution of totally abstaining CP patients compared to the Finnish population. All the differences were statistically significant ($p < 0.05$).

Discussion

Finland has one of the highest incidences of CP in Europe. However, no recent epidemiological data involving CP in Finland exists. Our aim was to investigate the current status and treatment of CP patients. The study reveals the burden of CP on the healthcare system: the patients with the most common aetiologies - alcohol and smoking - also are at higher risk of developing complications. Half of the patients continue smoking and drinking despite their diagnoses. These patients have poorer QOL and more complications. Women were more likely to totally abstain from alcohol.

Alcohol and smoking contributed to the majority of aetiologies of CP but a significant number of aetiologies remained unknown (21%). It is possible that at least some of these could have been caused by biliary microlithiasis [23]. It is also possible that these patients with unknown aetiologies have a genetic mutation causing CP, possibly some of the CP patients identified as having CP of alcohol origin have a genetic factor predisposing to the disease. Not everyone with the same lifestyle develops AP or CP. Those with a genetic cause behind pancreatitis have many clinical similarities with alcohol induced pancreatitis [24,25]. Even though having the same aetiology (alcohol) a low percentage of CP patients had developed liver cirrhosis, and similar findings have also been presented in an earlier study [26], This reason why only some of those who consume hazardous amounts of alcohol and who smoke develop CP might be explained with a genetic predisposition towards developing pancreatitis. More research is needed on this subject.

In the year 2017 the median age of death in Finland was 75 years for men and 81 years for women compared to 62 for males and 63 for females in our CP population [27]. In our follow-up there were more deaths among CP patients with financial difficulties, pancreatic pain and worse physical and cognitive functioning this not been recorded in previous studies.

We found that most of the CP patients continued smoking after their diagnosis (42% of all CP patients continued smoking and only 22% had stopped smoking). Similar findings have been reported elsewhere, with 50–63% patients continuing smoking after diagnosis and 25% were former smokers [28,29]. CP patients and medical professionals need to be educated about the risks of smoking. This means that not only alcohol consumption history but also smoking history should be elicited.

Despite continuing smoking, a significant number of CP patients according to our questionnaire abstained from alcohol: 42% versus general Finnish population 13% [22]. In a prospective cohort study from the United States (Machicado et al.) a similar trend was seen where 80% of CP patients abstained from alcohol [29]. In our study alcohol related CP was more susceptible to complications than non-alcohol related CP. Alcohol related CP had statistically significant higher rates of pseudocysts, calcifications and combined complications. In earlier research pseudocysts have been associated with alcohol related CP [30–32]. No current data on alcohol consumption after diagnosis was available, nor on how it effects QOL.

In our study CP patients with a higher AUDIT score had a worse QOL, functioning and symptoms (C30) but pancreatic symptoms (PAN26) were not more common except for hepatic symptoms in the AUDIT 16p plus group. In our study CP patients with alcohol consumption after their diagnosis in addition to having more complications have more pancreatic pain, although this difference did not reach statistical significance. There was a major group of CP patients who were still drinking heavily ((AUDIT +16) 16% vs. 3% controls), these patients could benefit from an intervention preferably early on, before AP progresses to CP [33–35]. No earlier comparison of AUDIT scores in CP and general population has so far been presented.

In our study, women were more likely to follow advice on abstinence. Abstinence remains a challenge in this patient group. In our clinical practice, information on the importance of abstinence was given during hospitalization and at discharge by a doctor and a nurse. Information about further supportive programmes for abstinence in primary health care was offered to the patients during hospitalization, and given if the patient was willing to receive this information. However, contacting the support providers in the primary health care was the patients' own responsibility.

In our study smokers had a slightly higher rate of calcifications and pseudocysts although this did not reach statistical significance. Earlier research has reported a connection between the risk of calcifications and smoking [36,37].

Our pseudocyst percentage was higher than that reported in most studies ((12–40%) vs. 58%) [38–40]. A probable cause behind this is that our study was conducted in a tertiary care hospital with more severe cases of CP and modern imaging (CT, MRI, US) being more precise and more easily available than before.

The number of endoscopic procedures (27%) performed was approximately the same as reported in other studies (23–37.7%) but surgical interventions - surgery for CP pain in particular - was fairly rare (9%), compared to other reports (11–39%). In a Hungarian study 18.6% of patients had surgical pseudocyst drainage versus our 4.7% and 11.1% had pancreatic decompression surgery versus 0.9% in our study population. Pancreatic decompression surgery for pancreatic pain is very rare in Finland [28,29,41,42].

The CP patients' quality of life was poor, and they have more symptoms than in the control population. In a Polish demographic study A. Mokrowiecka et al., 2010 [42]. With QLQ C-30 and Pan26, CP patients had even more severe symptoms and poorer QOL scores in all sections than in our study. However, in the Polish study there was a higher percentage of current smokers than in our study (84% vs. 49% respectively), which may explain the difference. In a cross-sectional study by S Han et al. CP patients who smoked had higher rates of depression, anxiety and poorer quality of life [43].

CP patients had an inferior quality of life and poorer functioning in all the parameters measured (cognitive, social, emotional, financial and physical) especially those patients who continue to drink and smoke have more pancreatic pain. Similar studies also corroborate that CP patients have inferior QOL and also shorter lower life expectancy, most probably due to pain, pancreatic insufficiency and complications [2,29,42,44–47]. In our findings CP patients who continue to smoke have more pancreatic pain, which could be due to pancreatic ischaemia [48]. CP patients who had higher AUDIT score had poorer functioning and more severe symptoms in the QLQ-C30 response but there was no statistically significant difference in the PAN26 responses except for hepatic symptoms. This differs from the studies by Mokrowiecka et al. and Wehler et al. [42,49].

In general, CP patients are treated by gastroenterologists and surgeons. In Finland surgeons perform most ERCP procedures, and thus the endoscopic and surgical interventions are considered simultaneously. In our study population pancreatic surgery for CP pain was rare and was mainly performed to rule out malignancies or to treat complications. Over half of our study population had recurrent AP. It is speculated that AP and CP are part of the same disease spectrum but not all who have AP develop CP. In a 2015 meta-analysis Sankaran et al. involving 14 studies only 36% of patients with recurrent AP develop CP [50,51].

The strength of this study is the prospectively gathered AUDIT scores and QOL questionnaires. Since we gathered data from all CP patients treated in our hospital region catchment area this study gives a good view of the aetiology, treatment and lifestyle of CP patients in Finland.

The weaknesses of the study include that the first part of our study was conducted retrospectively relying on the medical archives. Because of this, smoking was not always recorded accurately or at all. Thus, smoking could be even more common than stated for CP patients. Because our data comes from a tertiary care hospital we do not have records from CP patients treated in general medicine. The percentage of these patients remains unknown, but presumably these are pain-free CP patients without complications, as they have not been in contact with specialized health care. Our questionnaire provides current data about the quality of life and alcohol consumption of CP patients. The response rate, only 41%, was lower than expected.

In conclusion, our study provides current data about the complications, lifestyles and quality of life of CP patients. CP causes a burden on the health care system and also on the patients. CP patients are a diverse population of different ages and with multiple aetiologies. Each person should be treated individually according to morphological changes, pancreatic function and pain. Half of the patients continue smoking and drinking despite their diagnoses and this affects their QOL. In the CP patient population there seems to be more who are totally abstinent and more heavy drinkers than in general population.

According to current knowledge, the most important measure to halt the progression of CP would be to prevent acute phases and for patients to stop smoking. Currently this does not happen in many of the CP patients, and it would thus be beneficial to increase awareness among CP patients and medical professionals.

Declaration of competing interest

The authors have no conflicts of interest.

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References

[1] Lowenfels AB, Maisonneuve P, Cavallini G, Ammann RW, Lankisch PG, Andersen JR, et al. Prognosis of chronic pancreatitis: an international multicenter study. International Pancreatitis Study Group. Am J Gastroenterol 1994 Sep;89(9):1467–71.
[2] Lévy P, Domínguez-Muñoz E, Imrie C, Löhr M, Maisonneuve P. Epidemiology of chronic pancreatitis: burden of the disease and consequences. United European Gastroenterol J 2014 Oct;2(5):345–54.
[3] Tandon RK, Sato N, Garg PK. Chronic pancreatitis: Asia-Pacific consensus report. J Gastroenterol Hepatol 2002;17:508–18.
[4] Drewes AM, Bouwense SAW, Campbell CM, Ceyhan GO, Delhaye M, Demir IE, et al. Guidelines for the understanding and management of pain in chronic pancreatitis. Pancreatology 2017 Sep - Oct;17(5):720–31. https://doi.org/10.1016/j.pan.2017.07.006. Epub 2017 Jul 13.
[5] Raimondi S, Lowenfels AB, Morselli-Labate AM, Maisonneuve P, Pezzilli R. Pancreatic cancer in chronic pancreatitis; aetiology, incidence, and early detection. Best Pract Res Clin Gastroenterol 2010;24:349–58.
[6] Duell EJ, Lucenteforte E, Olson SH, Bracci PM, Li D, Risch HA, et al. Pancreatitis and pancreatic cancer risk: a pooled analysis in the international pancreatic cancer case-control consortium (PanC4). Ann Oncol 2012 Nov;23(11):2964–70. https://doi.org/10.1093/annonc/mds140.
[7] Ráty S, Sand J, Nordback I, Rinta-Kiikka I, Vasama K, Hagström J, et al. Tumor-like chronic pancreatitis is often autoimmune pancreatitis. Anticancer Res 2015 Nov;35(11):6163–6.
[8] Herreros-Villanueva M, Hijona E, Bañales JM, Cosme A, Bujanda L. Alcohol consumption on pancreatic diseases World. J Gastroenterol 2013 Feb 7;19(5):638–47. https://doi.org/10.1016/j.yexmp.2018.01.002.
[9] Kleeff J, Whitcomb DC, Shimosegawa T, Esposito I, Lerch MM, Gress T, et al. Chronic pancreatitis. Nat Rev Dis Primers 2017 Sep 7;3:17060. https://doi.org/10.1038/nrdp.2017.60.
[10] Schneider A, Löhr 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. J Gastroenterol 2007;42:101–19.
[11] Capurso G, Archibugi L, Pasquali P, Aceti A, Balducci P, Bianchi P, et al. Prevalence of chronic pancreatitis: results of a primary care physician-based population study. Dig Liver Dis 2017 May;49(5):535–9. https://doi.org/10.1016/j.dld.2016.12.024.
[12] Machicado JD, Dudekula A, Tang G, Xu H, Wu BU, Forsmark CE, et al. Period prevalence of chronic pancreatitis diagnosis from 2001-2013 in the commercially insured population of the United States. Pancreatology 2019 Sep;19(6):813–8. https://doi.org/10.1016/j.pan.2019.07.003.
[13] Sellers ZM, MacIsaac D, Yu H, Dehghan M, Zhang KY, Bensen R. Nationwide trends in acute and chronic pancreatitis among privately insured children and non-elderly adults in the United States, 2007-2014. Gastroenterology 2018 Aug;155(2):469–478.e1. https://doi.org/10.1053/j.gastro.2018.04.013.
[14] Yadav D, Timmons L, Benson JT, Dierkhising RA, Chari ST. Incidence, prevalence, and survival of chronic pancreatitis: a population-based study. Am J Gastroenterol 2011 Dec;106(12):2192–9. https://doi.org/10.1038/ajg.2011.328.
[15] Sand J, Välikoski A, Nordback I. Alcohol consumption in the country and hospitalizations for acute alcohol pancreatitis and liver cirrhosis during a 20-year period. Alcohol Alcohol 2009 May - June;44(3):321–5. https://doi.org/10.1093/alcalc/agn121.
[16] Jaakkola M, Nordback I. Pancreatitis in Finland between 1970 and 1989. Gut 1993;34:1255–60.
[18] Fitzsimmons D, Kahl S, Butturini G, van Wyk M, Bornman P, Bassi C, et al. Symptoms and quality of life in chronic pancreatitis assessed by structured interview and the EORTC QLQ-C30 and QLQ-PAN26. Am J Gastroenterol 2005 Apr;100(4):918–26.
[19] Michelson H, Bolund C, Nilsson B, Brandberg Y. Health-related quality of life measured by the EORTC QLQ-C30–reference values from a large sample of Swedish population. Acta Oncol 2000;39(4):477–84.
[20] Aromaa A, Koskinen S. Health and functional capacity in Finland : Baseline

results of the Health 2000 health examination survey. National Public Health Institute. B3/2002, http://urn.fi/URN. 951-740-262-7.
[21] Howse F, Harris S, Hedges E, George S, Pickering R, Johnson CD. Normal response data for the pancreatic cancer quality of life (QoL) assessment questionnaire EORTC QLQ-PAN26. Pancreas November 2006;33(4):469.
[22] Härkönen J, Savonen J, Virtala E, Mäkelä P. Drinking habits survey. THL (National Institute for Health and Welfare); 2017, ISBN 978-952-302-873-9. http://urn.fi/URN.
[23] Räty S, Pulkkinen J, Nordback I, Sand J, Victorzon M, Grönroos J, et al. Can Laparoscopic Cholecystectomy prevent recurrent Idiopathic acute pancreatitis? A prospective Randomized Multicenter Trial. 2015.
[24] Aghdassi AA, Weiss FU, Mayerle J, Lerch MM, Simon P. Genetic susceptibility factors for alcohol-induced chronic pancreatitis. Pancreatology 2015 Jul;15(4 Suppl):S23–31. https://doi.org/10.1016/j.pan.2015.05.476.
[25] Ballard DD, Flueckiger JR, Fogel EL, McHenry L, Lehman GA, Watkins JL, et al. Evaluating adults with idiopathic pancreatitis for genetic predisposition: higher prevalence of abnormal results with use of complete gene sequencing. Pancreas 2015 Jan;44(1):116–21. https://doi.org/10.1097/MPA.0000000000000225.
[26] Aparisi L, Sabater L, Del-Olmo J, Sastre J, Serra MA, Campello R, et al. Does an association exist between chronic pancreatitis and liver cirrhosis in alcoholic subjects? World J Gastroenterol 2008 Oct 28;14(40):6171–9. https://doi.org/10.3748/wjg.14.6171. 2008.
[27] Official Statistics of Finland (OSF): Deaths [e-publication]. ISSN=1798–2545. 2017. Helsinki: Statistics Finland [referred: 4.11.2018]. Access method: http://www.stat.fi/til/kuol/2017/kuol_2017_2018-04-27_tie_001_en.html.
[28] Szücs Á, Marjai T, Szentesi A, Farkas N, Párniczky A, Nagy G et al. Chronic pancreatitis: multicentre prospective data collection and analysis by the Hungarian Pancreatic Study Group. PLoS ONE, 12(2), e0171420. http://doi.org/10.1371/journal.pone.0171420.
[29] 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. Am J Gastroenterol 2017 Apr;112(4):633–42. https://doi.org/10.1038/ajg.2017.42.
[30] Suchsland T, Aghdassi A, Kühn K, Simon P, Lerch MM, Mayerle J, et al. Predictive factors for and incidence of hospital readmissions of patients with acute and chronic pancreatitis. Pancreatology 2015 May-Jun;15(3):265–70. https://doi.org/10.1016/j.pan.2015.03.008.
[31] Cannon JW, Callery MP, Vollmer Jr CM. Vollmer. Diagnosis and management of pancreatic pseudocysts: what is the evidence? J Am Coll Surg 2009 Sep;209(3):385–93. https://doi.org/10.1016/j.jamcollsurg.2009.04.017.
[32] Rasch S, Nötzel B, Phillip V, Lahmer T, Schmid RM, Algül H. Management of pancreatic pseudocysts—a retrospective analysis. PLoS One 2017 Sep 6;12(9):e0184374. https://doi.org/10.1371/journal.pone.0184374.
[33] Nikkola J, Laukkarinen J, Huhtala H, Sand J. The intensity of brief interventions in patients with acute alcoholic pancreatitis should be increased, especially in young patients with heavy alcohol consumption. Alcohol Alcohol 2017 Jul 1;52(4):453–9. https://doi.org/10.1093/alcalc/agx023.
[34] Lang MB, Segersvärd R, Grundsten M, Segerdahl M, Arnelo U, Permert J, et al. Management of alcohol use disorders in patients with chronic pancreatitis. JOP 2012 Nov 10;13(6):654–9. https://doi.org/10.6092/1590-8577/1037.
[35] 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. Clin Gastroenterol Hepatol 2016 May;14(5):738–46. https://doi.org/10.1016/j.cgh.2015.12.040.
[36] Imoto M, DiMagno EP. Cigarette smoking increases the risk of pancreatic calcification in late-onset but not early-onset idiopathic chronic pancreatitis. Pancreas 2000;21(2):115–9.
[37] 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. https://doi.org/10.1097/01.mpa.0000437324.52598.ee.
[38] Lévy P, Barthet M, Mollard BR, Amouretti M, Marion-Audibert AM, Dyard F. Estimation of the prevalence and incidence of chronic pancreatitis and its complications. Gastroenterol Clin Biol 2006 Jun-Jul;30(6–7):838–44.
[39] Hao L, Pan J, Wang D, Bi YW, Ji JT, Xin L, et al. Risk factors and nomogram for pancreatic pseudocysts in chronic pancreatitis: a cohort of 1998 patients. J Gastroenterol Hepatol 2017 Jul;32(7):1403–11. https://doi.org/10.1111/jgh.13748.
[40] Cavallini G, Frulloni L, Pederzoli P, Talamini G, Bovo P, Bassi C, et al. Long-term follow-up of patients with chronic pancreatitis in Italy. Scand J Gastroenterol 1998 Aug;33(8):880–9. https://doi.org/10.1080/00365529850171567.
[41] Machicado JD, Chari ST, Timmons L, Tang G, Yadav D. A population-based evaluation of the natural history of chronic pancreatitis. Pancreatology 2018 Jan;18(1):39–45. https://doi.org/10.1016/j.pan.2017.11.012.
[42] Mokrowiecka A, Pinkowski D, Malecka-Panas E, Johnson Clinical CD. Emotional and social factors associated with quality of life in chronic pancreatitis. Pancreatology April 2010;10(Issue 1):39–46. https://doi.org/10.1159/000225920.
[43] Han S, Patel B, Min M, Bocelli L, Kheder J, Wachholtz A, Wassef W. Quality of life comparison between smokers and non-smokers with chronic pancreatitis. Pancreatology 2018 Apr;18(3):269–74. https://doi.org/10.1016/j.pan.2018.02.012.
[44] 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 Mar;42(2):293–300. https://doi.org/10.1097/MPA.0b013e31826532e7.
[45] Olesen SS, Juel J, Nielsen AK, Frøkjær JB, Wilder-Smith OH, Drewes AM. Pain severity reduces life quality in chronic pancreatitis: implications for design of future outcome trials. Pancreatology 2014 Nov-Dec;14(6):497–502.
[46] Mokrowiecka A, Pińkowski D, Małecka-Panas E. Assessment of quality of life in patients with chronic pancreatitis. Med Sci Monit 2011 Oct;17(10):583–8.
[47] Olesen SS, Frandsen LK, Poulsen JL, Vestergaard P, Rasmussen HH, Drewes AM. The prevalence of underweight is increased in chronic pancreatitis outpatients and associates with reduced life quality. Nutrition 2017 Nov - Dec;43–44:1–7. https://doi.org/10.1016/j.nut.2017.06.019. Epub 2017 Jul 6.
[48] Pham A, Forsmark C. Chronic pancreatitis: review and update of etiology, risk factors, and management. F1000Res 2018 May 17;7. https://doi.org/10.12688/f1000research.12852.1. pii: F1000 Faculty Rev-607.
[49] Wehler M, Nichterlein R, Fischer B, Farnbacher M, Reulbach U, Hahn EG, et al. Factors associated with health-related quality of life in chronic pancreatitis. Am J Gastroenterol 2004 Jan;99(1):138–46.
[50] Ahmed Ali U, Issa Y, Hagenaars JC, Bakker OJ, van Goor H, Nieuwenhuijs, et al. Risk of recurrent pancreatitis and progression to chronic pancreatitis after a first episode of acute pancreatitis. Clin Gastroenterol Hepatol 2016 May;14(5):738–46. https://doi.org/10.1016/j.cgh.2015.12.040. Epub 2016 Jan 6.
[51] 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 Nov;149(6):1490–1500.e1. https://doi.org/10.1053/j.gastro.2015.07.066. Epub 2015 Aug 20.