Nutritional Management of Chronic Pancreatitis

Nutritional Management of Pancreatic Disease Virtual Study Day

Edel Carty Senior Dietitian 2/11/2021

Declaration of Interest: Honoria received for presenting from Viatris

Overview

- What is Chronic pancreatitis?
- Drivers of malnutrition in Chronic Pancreatitis
- Nutritional assessment and management
- Diagnosing Pancreatic exocrine insufficiency
- Pancreatic enzyme replacement therapy

Abbreviations

CP = Chronic Pancreatitis

- **PEI** = Pancreatic Exocrine Insufficiency
- **PERT** = Pancreatic Exocrine Replacement Therapy
- **ESPEN** = European Society for Enteral and Parenteral Nutrition
- **EN** = Enteral Nutrition
- **ONS** = Oral Nutrition Supplements
- **PN** = Parenteral Nutrition
- NJ = Naso jejunal
- FE-1 = Faecal Elastase
- **BMI** = Body Mass index

ESPEN Guidelines

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ESPEN Guideline

ESPEN guideline on clinical nutrition in acute and chronic pancreatitis



NUTRITIC

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BMJ Open Gastroenterology

Consensus for the management of pancreatic exocrine insufficiency: UK practical guidelines

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ABSTRACT

Introduction Pancreatic exocrine insufficiency is a finding in many conditions, predominantly affecting those with chronic pancreatitis, pancreatic cancer and acute necrotising pancreatitis. Patients with pancreatic exocrine insufficiency can experience gastrointestinal symptoms, maldigestion, malnutrition and adverse effects on quality of life and even survival.

There is a need for readily accessible, pragmatic advice for healthcare professionals on the management of pancreatic exocrine insufficiency.

Methods and analysis A review of the literature was conducted by a multidisciplinary panel of experts in pancreatology, and recommendations for clinical practice were produced and the strength of the evidence graded. Consensus voting by 48 pancreatic specialists from across the UK took place at the 2019 Annual Meeting of the Pancreatic Society of Great Britain and Ireland annual scientific meeting.

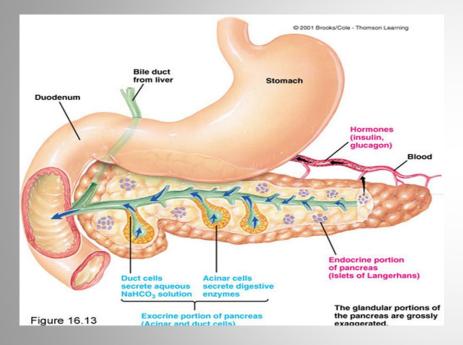
Results Recommendations for clinical practice in the diagnosis, initial management, patient education and long term follow up were developed. All recommendations achieved over 85% consensus and are included within these comprehensive guidelines.

with improved survival and quality of life (QoL) in patients with PEL.^{8–10}

PEI may be underdiagnosed and undertreated in the UK, as demonstrated in other European countries.¹¹ Patient support groups report management of PEI as the most common concern raised on their patient helpline (Pancreatic Cancer UK, 2015), and 'difficulty in managing GI problems, diet and digestion' are documented as the primary unmet need in patients with pancreatic cancer (PC).¹² In addition, patients with chronic pancreatitis (CP) feel unsupported by healthcare professionals (HCPs) in the management of PEI (Pancreatitis Supporters Network, 2015). Consequently, there is a need for readily accessible, pragmatic advice for both specialist and non-specialist HCPs. The aim of this article is to provide evidencebased guidance on the diagnosis and management of PEI, including differential diagnosis and follow-up. This article does not make detailed recommendations regarding the management of cystic fibrosis (CF) as this is

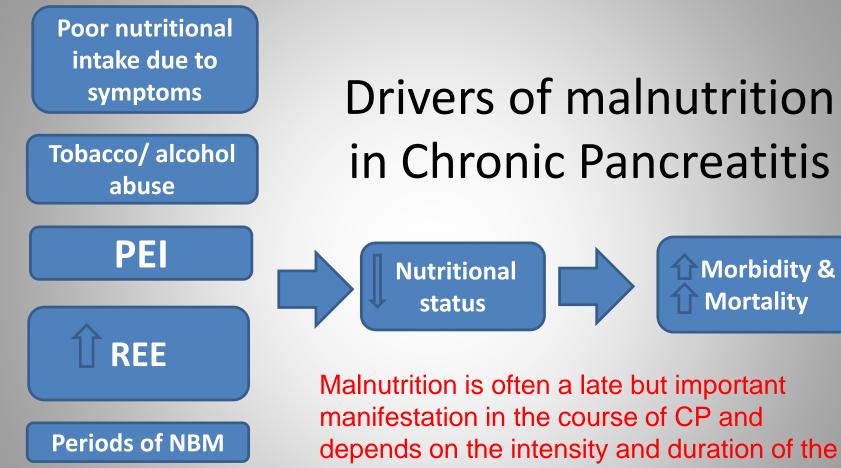


Chronic Pancreatitis (CP)



Chronic pancreatitis is a disease with progressive and irreversible inflammatory changes in the pancreas that result in permanent structural damage with fibrosis, which can lead to impairment of exocrine (PEI) and often endocrine function.

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underlying disease

ESPEN 2020

Malnutrition in CP

22-94% prevalence rates for PEI – due to wide range of PEI markers used in studies ESPEN 2020

26% of patients underweight

Olesen 2017

Sarcopenia present in 17%

Olesen 2017

>50% overweight/obese however had lower muscle stores & reduced hand grip strength
Duggan et al 2014

Dietetic aims

The main goals of nutritional therapy are to:

- Prevent undernutrition/ improve nutritional status
- Reduce symptoms of maldigestion +/malabsorption
- Prevent micronutrient deficiencies

Nutritional Management of CP

- Effective management of pain and abstinence from alcohol can improve nutritional status on their own
- 80% of patients can be managed with normal food supplemented by PERT
- **10-15%** will require **ONS**
- 5% of patients will require EN

Gianotti et al 2009

• <1% of patients will require PN

Gianotti et al 2009

Food first

- Dietary counselling as effective as ONS at improving CP patient's nutritional status Singh et al 2008
- No need for dietary fat restriction unless steatorrhoea cannot be controlled
 ESPEN 2020
- CP patients with normal nutritional status (usually early stage) should adhere to a well balanced diet
 ESPEN 2020

 Malnourished patients should be advised to consume high protein, high energy food in five to six small meals per day
 ESPEN 2020

 High fibre diets are not recommended as they may inhibit PERT, and result in malabsorption
 Dutta 1985

ONS and CP

- Oral nutrition support with dietary counselling is usually sufficient to improve nutritional status
 Singh et al 2008
- ONS should be prescribed to undernourished patients only if oral nutrition is insufficient for reaching the calorie and protein goals
- If ONS is indicated:
 - Whole protein ONS should be gradually increased with PERT if required
 - If not tolerated could try peptide, MCT based ONS





Meier et al, 2002

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Enteral nutrition (EN)

- EN is indicated if patients with malnutrition are not responding to oral nutrition support
- NJ should be used in patients with pain, delayed gastric emptying, persistent nausea or vomiting and gastric outlet syndrome ESPEN 2020
- Semi- elemental formulas with MCT can be used if standard formulas are not tolerated
 ESPEN 2020

*Note in SHSCT semi-elemental feeds generally used first line

If no improvement with MCT formulae, PERT should be introduced alongside

Ferrie 2011

Parenteral nutrition (PN)

- PN may be indicated in patients with
 - Gastric outlet obstruction
 - A need for gastric decompression
 - No enteral access to the jejenum
 - Complex fistulating disease
 - Intolerance to EN or full needs cannot be met enterally

Micronutrient supplementation

- Insufficient evidence to suggest routine/ blind supplementation of micronutrients in absence of malabsorption
- Monitor and supplement if low concentrations detected or if clinical signs of deficiency occur:
 - Fat soluble vitamins: A, D, E & K
 - Water soluble vitamins: B12, folic acid & thiamine
 - Minerals: Magnesium, iron, selenium and zinc

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• In community setting may be difficult to obtain micronutrient screen

Bone Health & CP

- The prevalence of osteoporosis is 1 in 4 and 2 out of 3 can experience osteopathy
 Duggan et al 2014
- Offer a DEXA every 2 years
- Basic preventative measures:
 - Optimise Calcium and Vitamin D sources
 - Correct dosing of PERT
 - Regular weight bearing exercise
 - Smoking/ alcohol cessation

Phillips et al 2021

Lohr et al 2017

Nutritional requirements in CP

	Requirements
Energy	25kcal/ kg BMI 18.5-30kg/m2 and <65 years (Dickerson et al, 1991)
Protein	1-1.5g/kg/day (Imrie et al, 2010)
Fat	No need for fat restriction unless symptoms of steatorrhea cannot be controlled (ESPEN 2020) 30% of total calories can be given as fat (Duggan et al, 2010) Supplementation with MCT fat source may be useful (Giger et al, 2004, Duggan et al, 2010) with gradual introduction and monitoring
Carbohydrate (CHO)	Diets rich in CHO advised unless CP concurrent with Diabetes (Duggan et al 2010)
Fibre	Very high fibre diets (>25g/day) are not recommended as they may absorb enzymes and delay nutrient absorption (Dutta 1985)
Fat soluble vitamins (A,D,E &K) and micronutrients	Micronutrient deficiencies are prevalent in patients with CP (Sikkens et al, 2013; Duggan et al, 2014). Should be assessed and monitored with supplementation, if deficiencies are present (Duggan et al, 2010, Lohr et al, 2017)
Alcohol	Life long abstinence recommended

PEI

Globally agreed definition across pancreatic societies:

PEI is defined as a reduction of pancreatic exocrine activity in the intestine at a level that prevents normal digestion Hoffmeister 2015, Toouli 2010

The most common cause of PEI is CP due to loss of pancreatic parenchyma and reduced secretion Phillips et al 2021

22-94% of prevalence rates for PEI – due to wide range of PEI markers used in studies ESPEN 2020

PEI may go undetected because the signs and symptoms are similar to those of other gastrointestinal disease

The degree of PEI correlates with disease severity

Dumasy et al 2004

Steatorrhoea may not become apparent until greater than 90% of pancreatic function is lost DiMagno et al, 1973

Diagnosing PEI in CP

A number of factors need to be considered to reliably diagnose PEI:

- GI symptoms
- Anthropometry
- Nutritional Deficiencies
- Stage of CP
- CT Findings
- Faecal Fat Testing

GI Symptoms of PEI - Steatorrhoea

- Loose watery yellow/orange stool
- Floats / difficult to flush away
- Oily / visible food particles

VERY LATE SYMPTOM



However... these symptoms can often be masked by other medications and self imposed fat restrictions

Other GI / Clinical Symptoms of PEI

- Large volume stool
- Undigested food in the stool
- Post-prandial abdominal pain
- Offensive smelling stools
- Nausea / colicky abdo pain
- GORD
- Bloating/flatulence
- Weight loss despite good oral intake
- Vitamin deficiencies (especially A, D, E, K)
- Hypoglycaemia in patients with Diabetes

O'Keefe et al 2001, Genova Diagnostics 2008, Freiss & Michalski 2009

Anthropometry in Diagnosing PEI

- There is no agreed diagnostic % weight loss for PEI
- A single BMI measurement is of limited diagnostic use on its own and can be normal in patients with PEI
- BMI should always be interpreted with caution in an obese population
- Evidence for recording specific anthropometric measurements is poor or absent for patients with PEI with limited data in CP

Phillips et al 2021

• I feel % weight loss is the most useful anthropometric calculation to aid with diagnosing PEI

Nutritional Deficiencies in Predicting PEI

Low levels of vitamin E reported in CP patients with PEI or steatorrhoea

Kalvaria 1986, Marotta 1994, Nakamura 1996

Retinol-binding protein (a marker of vitamin A status) may be lower in patients with alcohol induced CP and steatorrhoea vs patients with CP alone. Marotta 1994

Magnesium and zinc deficiency have been reported in CP, but not specifically in patients with PEI Lindkvist 2012, Vujasinovic 2019

Vitamin D deficiency has been shown to have a high incidence in CP (53%–66%) but no significant difference when PEI is present. Duggan 2014, Marotta 1994, Sikkens 2013, Dutta 1982

Given the evidence available, no finding is specific enough to recommend using serum micronutrients alone as a diagnostic marker for PEI.

Nutritional Deficiencies in Predicting PEI

Most Sensitive Nutritional Markers:

- Low Magnesium
- Low Vitamin E
- Low Retinol Binding Protein / Vitamin A

Phillips 2021

"The higher the number of nutritional deficiencies the higher the chance of PEI"

Professor Dominguez-Munoz 2019

Stage of CP in diagnosing PEI

The latency between onset of first symptoms and signs of CP, including pain and malabsorption / malnutrition is between 5-10 years in alcoholic, but delayed in non-alcoholic CP Hao 2018

PEI is reported in 94% of patients within 10 years of CP onset

Dumasy 2004

In CP, progressive destruction of the pancreatic tissue results in PEI Keller 2005

Basically the longer the patient has CP, the higher the likelihood of PEI given its progressive nature

CT Findings in diagnosing PEI

Morphological changes of CP including calcification and main pancreatic duct dilatation can be identified on CT scanning

Pancreatic calcification is a late/severe feature of CP with PEI present in 50% of patients with substantial calcification Scuro 1990, Lankisch 1986

47% of patients with severe PEI & CP were shown to have significant atrophy and ductal dilatation on CT Malfertheiner 1986,1989

Therefore, although radiological evidence of pancreatic morphological abnormalities is supportive of a diagnosis of PEI, further evidence is required.

Faecal Elastase (FE-1)

- Several tests for PEI exist eg Coefficient of fat absorption, indirect C-labelled mixed triglyceride breath test
- FE-1 is used in clinical practice less invasive & readily available
- Only small sample of faeces required
- Stable at room temperature for 3 days
- The lower the FE-1 concentration, the higher the probability of PEI.

Dominguez-Munoz et al 2017

Faecal Elastase

 Analysed in RVH Paediatric Biochemistry Lab (Ph 9063 2148/3064)

• Ideally should be a formed motion to suit sample technique!!

 Type 7 BO can be analysed but likely result will be "Not Reportable"

• Watery sample can cause a false positive result! Consider repeat!

Community Faecal Elastase Testing

- Recently some GPs refusing to organise FE-1 unless a labelled request form received from Referring Consultant
- Not all patients requiring FE-1 have a Consultant!
- Dietitian can interpret results!

Way Forward:

Discussion with GI Consultant and GP Representative re potential role of the Dietitian as the Referrer



Faecal Elastase Test

Sensitivity

- 82-100% in severe pancreatic disease
- 33-100% in moderate pancreatic disease
- 25-65% in mild pancreatic disease

Specificity

• 55-100% in mild pancreatic disease

Detection

- < 200ug/g stool moderate pancreatic disease
- < 100ug/g stool severe pancreatic disease

Phillips 2021

Dig Dis Sci DOI 10.1007/s10620-017-4524-z



REVIEW

Potential for Screening for Pancreatic Exocrine Insufficiency Using the Fecal Elastase-1 Test

J. Enrique Domínguez-Muñoz $^1\cdot$ Philip D. Hardt $^2\cdot$ Markus M. Lerch $^3\cdot$ Matthias J. Löhr 4

"Physicians should be aware that an exact cut-off of FE-1 levels for PEI in different clinical scenarios cannot be established, and that <u>FE-1 levels should be considered together with an appropriate evaluation of symptoms, signs, and nutritional status</u>". "FE-1 level of 200-250 is likely not normal. 500 is normal"

Dominguez-Munoz et al 2017

Considered alone FE-1 shows a problem with enzyme secretion only

Dominguez-Munoz – Masterclass 2019

When is FE-1 required/ not required in CP?

Required

- Patients with GI symptoms of maldigestion with or without known associated conditions
- Maldigestion symptoms: steatorrhoea, wt loss, diarrhoea, abdo pain or bloating
- Associated conditions: patients with coeliac disease, IBS, HIV, Type 1 DM and acute severe pancreatitis after initial presentation

Not Required

- Steatorrhoea / malabsorption symptoms in pts with CP with dilated pancreatic duct or severe pancreatic calcification
- Severe necrotising Pancreatitis
- Post-op Total Pancreatectomy

Phillips et al 2021

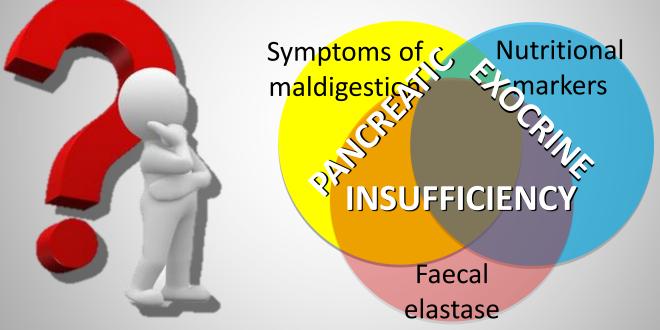
My opinion:

In early/mild CP consider FE-1 if symptoms non specific

PEI reported in 94% of patients within <u>10 years</u> of CP onset so FE-1 not then required

Dumasy 2004





Domínguez-Muñoz & Phillips 2018

Combined Factors for PEI

Consider all factors in pie chart in patients with any condition or disease potentially causing PEI +/- changes in anthropometry + poor Glycaemic Control in patients with DM.

- Abnormal FE-1 alone = Not PEI. Check other factors
- Abnormal FE-1 and Symptoms of Maldigestion most likely PEI
- Normal FE-1 and Symptoms of Maldigestion = Not PEI (? Bacterial overgrowth)
- Abnormal FE-1 and Abnormal Nutritional markers = Most likely PEI
- Normal FE-1, Symptoms of Maldigestion and Abnormal Nutritional markers = Most likely PEI as FE-1 can be falsely negative
- Abnormal FE-1, Symptoms of Maldigestion, and Abnormal Nutritional markers = Definite PEI
 Prof Dominguez-Munoz Masterclass 2019

PERT

- PERT is the mainstay treatment of PEI
- All products derived from pigs! Non-porcine products failed in Phase III clinical trial. Jewish and Muslim faith Leaders consent to its use as no available alternative
- "Creon is the only available PERT with mini microspheres so is the most superior PERT for the treatment of PEI" Prof Dominguez-Munoz quote 2019
- Creon generally used first line

The addition of PPI

- The addition of PPI can be beneficial if PERT is not effective, as PERT may be inhibited by gastric acid
- However data is not consistent
- Given conflicting data and potential for long-term complications of PPI use eg

C-diff, low Mg, nausea and diarrhoea, the addition of PPI is a second-line treatment

Phillips 2021

Treatment of PEI

Modified from Domínguez-Muñoz, Clin Gastroenterol Hepatol 2011 Pancreatic exocrine insufficiency secondary to any pancreatic or extrapancreatic disease or Success: condition Absence of Enteric-coated pancreatin mini-microspheres (50,000-75,000 Ph.U lipase/meal; maldigestion-25,000-50-000 Ph.U./snack) related Add PPI (bd) symptoms Normal Increase enzyme dose (up to double the dose) nutritional Check for other causes of evaluation maldigestion/malabsorption and treat

PERT

- Like CP, exocrine insufficiency is progressive and doses escalate with time
- Some patients need really high doses (> 150, 000 units with a meal = > 25 capsules / day = 9-10 x 100 cap tubs per month)
- Significant pill burden
- Treat like insulin different doses for different patients for different meals

What if symptoms do not improve?

- ? Adequate dose minimum dose 50 000 with meals and 25 000 per snack. Consider increasing dose.
- **? Correct timings ? Divided doses** spreading PERT throughout a meal rather than consuming before or after a meal
- **?** Able to swallow if capsules unable to be swallowed, they should be opened, placed on an acidic puree (eg fruit puree/ fruit yogurt/ juice ONS) and swallowed at intervals. Granules should not be chewed or crushed, as this removes the enteric coating, resulting in premature activation of the enzymes. The mouth should be rinsed with cool water to prevent ulceration
- ? PPI. Initially introduce once daily. May require twice daily!

What if symptoms do not improve?

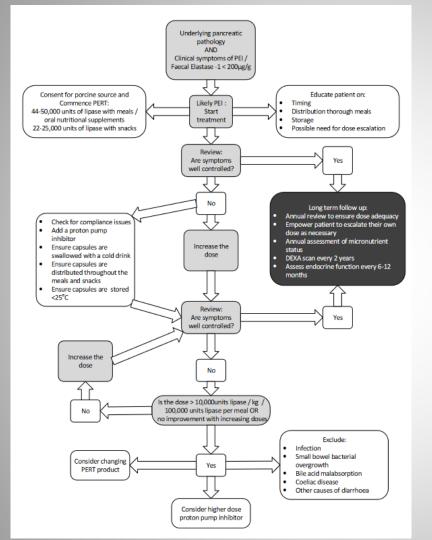
? Compliance with advice – should be swallowed with a cold drink. Ensure capsules are stored at <25°C

? Alternative PERT product needed – consider alternative eg Nutrizym, Pancrex V, Pancrease if the dose is >10,000 units lipase/kg/day or 100,000 units lipase per meal or no improvement with increasing doses. No maximum dose proposed for adults

? Exclude other causes if exceeding above doses – such as infection / SBBO / BAM / Coeliac Disease / other causes of diarrhoea

Routine Follow-up of patients with PEI

- Annual review to ensure PERT dose adequacy
- Empower patient to escalate their own PERT dose as necessary
- Annual assessment of micronutrient screen
- DEXA scan every 2 years as high prevalence of Osteoporosis and Osteopenia with PEI
- Assess endocrine function every 6-12 months



Pg 11, Phillips et al 2021

Table 5

Nutritional assessment in the patient with chronic pancreatitis.

Anthropometric	Biochemical	Symptom	Body
	assessment	assessment	composition
 Change in body weight Functional assessment: Hand-grip strength dyna- mometry/6-min walk tests/sit to stand tests. Skin fold thickness, waist circumference and mid arm muscle circumference. Presence of ascites/edema 	 Fat soluble vitamins (A, D, E, K) Bone health (Parathyroid hormone) Trace elements (magnesium, selenium, zinc) Anemia screen (iron studies, B12, folate, ferritin and CRP) Glycemic control: HbA1c and random glucose 	 Change in dietary intake Appetite Presence of symptoms that impact on oral intake (nausea/ pain/indigestion/ early satiety) Presence of exocrine/ endocrine dysfunction 	 CT/US imaging of muscle stores (muscle mass) DXA scanning (bone mineral density)

CRP = C-reactive protein, HbA1c = hemoglobin A1c, CT = computed tomography, US = ultrasound, DXA = dual-energy X-ray absorptiometry.

Take Home Messages

- Chronic pancreatitis is a disease with progressive and irreversible inflammatory changes
- Malnutrition is often late in the course of CP & depends on the intensity & duration of the underlying disease
- The most common cause of PEI is CP
- A number of factors need to be considered to reliably diagnose PEI
- Permission should be given to patients to dose escalate PERT
- Micronutrient supplementation should be proposed to patients with known malabsorption
- Appropriate therapy improves outcomes.

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