Early chronic pancreatitis - Are you missing it?

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Pancreatic diseases and Pancreatic Exocrine Insufficiency (PEI)
What is the relevance to general practice?

Objectives:
- Pancreatic diseases
  - Chronic pancreatitis
  - Pancreatic cancer
  - Post pancreatectomy
- Pancreatic exocrine insufficiency (PEI)
  - Often under diagnosed
  - With potentially severe consequences

If my patient has the non-specific symptoms:
- abdominal pain
- diarrhoea
- weight loss
Should I be considering pancreatic disease and pancreatic exocrine insufficiency (PEI)?

Shared GI symptoms

Pancreatic disease and Pancreatic Exocrine Insufficiency (PEI)
What is Pancreatic Exocrine Insufficiency (PEI)?

PEI and chronic pancreatitis

PEI and pancreatic cancer

Does pancreatic disease exist undiagnosed?

Pancreatic exocrine insufficiency (PEI)
Pancreatic cancer
Chronic Pancreatitis

The historical data

Does chronic pancreatitis exist undiagnosed?

- A study of 394 consecutive autopsies conducted in Denmark (1978)
- Histological examination of the pancreas organ
- 13% (52) have histological features consistent of chronic inflammation
- Only 0.5% (2) of these patients had a diagnosis of chronic pancreatitis
Evidence for undiagnosed pancreatic disease and PEI in the general population

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<tr>
<th>Study author</th>
<th>Country</th>
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<th>Method of investigation</th>
<th>Period</th>
<th>PEI</th>
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Why does chronic pancreatitis exist undetected?

- 90% of patients with alcoholic chronic pancreatitis presents with mild, moderate or no pain symptoms
- Alcohol-related chronic alcoholics have a higher frequency of chronic pancreatitis with mild, moderate or no pain symptoms
- 20% of patients with idiopathic chronic pancreatitis presents with mild, moderate or no pain symptoms

A substantial time lag occurs between symptom presentation to diagnosis of pancreatic cancer

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<th>Symptom presentation to primary care in UK, within 2 years prior to diagnosis of pancreatic cancer</th>
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<td>Abdominal pain, Jaundice, Change in bowel habit, Weight loss, Fatigue</td>
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<tr>
<td>Nausea, Vomiting, Fever, sweats</td>
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The consequences of undiagnosed pancreatic disease

- Increased risk of pancreatic cancer
- Increased risk of diabetes
- Increased risk of osteoporosis
- Malnutrition
- Reduced quality of life

Consequences of undiagnosed/untreated disease

- Pancreatic Exocrine Insufficiency (PEI)
- Pancreatic cancer
- Chronic pancreatitis

Aetiology of chronic pancreatitis

- Non-alcoholic (55%)
- Non-alcoholic (45%)

NAPS2: a higher than expected number of CP patients (55%) were classified with non-alcoholic aetiology

North American Pancreatitis Study 2 (NAPS2)
Clinical consequences of PEI

Qualitative research conducted by the NSW Cancer Council, in 61 people including patients diagnosed with pancreatic cancer, carers, family members, and bereaved participants.


Participants identified that their priority unmet supportive care need was their difficulty in managing gastrointestinal problems, diet and digestion. They expressed strong feelings of frustration and anger relating to struggling with symptoms of PEI.

“I just can’t get enough nutrition you know…”
- Patient, female

“I found this very confronting, her not wanting to eat. I (crying) try to force feed her. She gets upset, it makes it worst.”
- Carer, male (Dad)

“You’ve got this lack of food intake. I can’t eat as much of what I used to and there are things that I can’t eat.”
- Patient, female

Is early detection of chronic pancreatitis and pancreatic cancer possible?

Curable (operable) lesions and localised non metastatic tumors are detectable using technologies currently used in clinical practice

Endoscopic ultrasound (EUS)
MRI
Computed tomography

American Pancreatic Association guidelines for diagnosis of chronic pancreatitis

How is PEI detected?

Direct tests:
- Secretin-caerulein tubular test

Indirect tests:
- 3 day faecal fat test
- Faecal elastase-1 stool test
- 13C mixed triglyceride breath test
Faecal elastase-1 Stool Test

- Faecal elastase-1 test is becoming more common in clinical practice.
- In 2010, it was reported to be the most popular test used to evaluate PEI.
- Requires a single formed stool sample.
- Measures the elastase concentration in the stool.
- Specificity: approximately 93%.

>200 µg/g stool: normal value
<200 µg/g stool: mild PEI
<100 µg/g stool: severe PEI


PEI Diagnostic pathway

PEI Diagnostic pathway

Treatment of PEI

Pancreatic Enzyme Replacement Therapy (PERT)

PERT treatment goals

- eliminate maldigestion
- eliminate malabsorption
- maintain adequate nutrition

1. Toouli et al. MJA 2010; 193; 461-467

Recommendations to investigate for pancreatic disease and PEI in patients presenting with chronic diarrhoea symptoms
International guidelines for management of PEI in pancreatic cancer patients

Delivery of pancreatic enzymes using a modern oral formulation

1. The capsule containing pancreatic enzymes enters the stomach along with the food.
2. The outer capsule dissolves rapidly to release enteric coated mini-microspheres which mix with the chyme.
3. The mini-microspheres with particle size of 0.7–1.6 mm pass through the pylorus together with the chyme.
4. The active digestive enzymes are released in the duodenum to digest nutrients.

Effects of PERT on GI symptoms (PEI in Chronic Pancreatitis)

Patients on pancreatic enzyme therapy (Creon) showed a clinically significant response:
- Stool frequency reduced from 6 to 1.5 per day (p<0.002)
- Stool consistency changed from “diarrhoea” to “normal” (p<0.002)

Observational study involving 19 patients identified with PEI using the faecal elastase test. Patients were treated with Creon 30,000 units lipase with meals for 12 weeks. Patient symptoms were recorded using Bristol stool scale and the number of stools per day.

Effects of PERT on fat malabsorption in patients with pancreatic exocrine insufficiency post pancreatic surgery

A randomised, double blind, placebo controlled study over 7 days. PERT significantly improves fat absorption by 35% after one week.

58 patients with pancreatic exocrine insufficiency after pancreatic resection due to malignancy or chronic pancreatitis.

Seiler C. et al, Aliment Pharm & Ther, 2013

Effects of PERT on the quality of life (QoL) of patients with chronic pancreatitis

PERT significantly improved QoL of patients in terms of:
- Physical function
- Social function
- Emotion
- Medical treatment
- GI Symptoms
- diarrhoea/steatorrhoea
- abdominal pain
- nausea
- vomiting
- weight loss

Observational prospective, multicentre study which assessed symptom and quality of life over one year in patients with newly diagnosed PEI associated with chronic pancreatitis without prior pancreatic enzyme treatment. Quality of life was assessed using gastrointestinal quality of life index (GIQLI).

Effects of PERT on body weight and nutritional status

Observational study over 12 months, n=23
PERT adult dose range

Maximum dose recommended by:

Management of PEI using PERT

PERT:
- Initially – 25,000 to 40,000 units lipase with each meal
- Encourage patients to eat 6 smaller meals per day rather than 3 large meals
- If required, increase dose up to 60,000 lipase units with each meal

Other considerations:
- Patient compliance
- Many patients have acidic intestinal pH which decrease enzyme release from preparations which have pH sensitive enteric coating
  - Acid suppressing agents may be required in some patients
- Lack of weight gain due to inadequate fat intake
  - Fat restriction may require use of PERT

Summary

- Pancreatic diseases and PEI have similar GI symptoms
- PEI is associated with exocrine (and endocrine pancreatic) diseases including chronic pancreatitis and pancreatic cancers
- PERT is the main treatment option for PEI
- PERT provides symptomatic benefit and improved QoL for those patients with pancreatic insufficiency
- Clinicians should be aware of the problem of under diagnosing these conditions
  - and have a low threshold for checking FEL-1 and assessing pancreatic insufficiency of patients