Editorial Commentary

Optimizing management of patients with pancreatic exocrine insufficiency

Marianna Arvanitakis^, Alia Hadefi^, Michael Fernandez Y. Viesca

Department of Gastroenterology, HUB, Erasme University Hospital-Université Libre de Bruxelles, Brussels, Belgium

Correspondence to: Marianna Arvanitakis. Department of Gastroenterology, HUB, Erasme University Hospital-Université Libre de Bruxelles, Brussels, Belgium. Email: marianna.arvanitaki@erasme.ulb.ac.be.

Comment on: Phillips ME, Hopper AD, Leeds JS, *et al.* Consensus for the management of pancreatic exocrine insufficiency: UK practical guidelines. BMJ Open Gastroenterol 2021;8:e000643.

Keywords: Pancreas; chronic pancreatitis; steatorrhea; maldigestion; pancreatic surgery

Submitted Dec 26, 2022. Accepted for publication Jan 05, 2023. Published online Jan 09, 2023.
doi: 10.21037/hbsn-22-635
View this article at: https://dx.doi.org/10.21037/hbsn-22-635

Pancreatic exocrine insufficiency (PEI) is related to decreased pancreatic enzyme availability and/or activity (1). Multiples underlying mechanisms can cause PEI, such as loss of functioning parenchyma (chronic pancreatitis, pancreatic resections, pancreatic cancer...), decreased secretion despite intact parenchyma (obstruction of the pancreatic duct, decreased endogenous stimulation, intraduodenal inactivation of pancreatic secretions), and asynchrony (gastric resections, Roux-en-Y gastric by-pass) (1). Patients with PEI can present with non-specific gastrointestinal (GI) symptoms suggesting maldigestion, including steatorrhea, weight loss, abdominal pain, and bloating (2). Due to the character of the symptoms, as well as to the potential diversity of the underlying disease, PEI is underdiagnosed, instauration of treatment may be delayed, and overall management not optimal (3,4). Furthermore, PEI can have a negative impact of outcome (5) and pancreatic enzyme replacement therapy (PERT) can improve both survival and quality of life (QoL) (6,7). These findings highlight the importance of the current UK practical guidelines for the management of PEI, which include an evidence-based review, as well as a consensus based on voting from a multidisciplinary panel of experts in pancreatology (8). Moreover, the national character of the work allows adapting the recommendations to the UK health care framework and therefore offer readily accessible, pragmatic advice for both specialist and non-specialist health care professionals (HCP).

Main points of the guidelines include statements on definition and diagnosis of PEI, etiology, therapeutic management including treatment failure, potential adverse events, and long-term follow-up (8). The measurement of fecal elastase 1 (FE1) in a stool sample is widely applied in clinical practice for diagnosis of PEI but has low sensitivity in patients with mild PEI and can yield false positive results in case of water contamination or watery diarrhea (9). Exploring additional markers for malnutrition (anthropometric measurements, micronutrients levels) can further support the diagnosis of PEI (8). When considering etiology, pancreatic diseases such as chronic pancreatitis, pancreatic cancer, previous pancreatic surgery, or PEI following severe acute necrotizing pancreatitis should be explored; nevertheless, less common causes such as type I diabetes mellitus, coeliac disease, previous gastrectomy or Roux-en-Y gastric by-pass should be kept in mind (8,9). PERT is the cornerstone of management, but adequate dosage and optimal consumption during meals are crucial for treatment response (2,8,10). The authors also provide practical guidance for specific cases such as patients with difficulty swallowing, receiving enteral nutrition and during pregnancy and breastfeeding (8). PERT is well tolerated and has scarce adverse events in adults, therefore dosage can be increased in case of limited symptom improvement (8).

^ ORCID: Marianna Arvanitakis, 0000-0001-7112-4282; Alia Hadefi, 0000-0002-6595-2809.

Table 1 Research questions in the field of pancreatic exocrine insufficiency

Stage	Questions
Diagnosis	• Increase sensitivity of FE1 even for patients with mild PEI and allow early diagnosis before clinical symptoms
	• Develop alternative noninvasive, accessible, and easily available diagnostic methods
PERT	• Assess impact of PERT on prognosis for patients with PEI related to pancreatic cancer
	• Evaluate effect of PERT for patients with PEI related to extrapancreatic causes (ex., following gastrectomy or Roux-en-Y gastric by-pass)
	• Establish modalities for PERT administration in patients with exclusive enteral nutrition
	• Establish systemic step-by-step approach in case of initial treatment failure
Follow-up	• Assess safety regarding long term utilization of PERT
	• Evaluate effect of PERT on bone health

FE1, fecal elastase; PEI, pancreatic exocrine insufficiency; PERT, pancreatic enzyme replacement therapy.

Furthermore, proton pump inhibitors can be added in case of persistent treatment failure (8). Finally, in case of ongoing symptoms despite adequate dosage and proton pump inhibitor therapy, other conditions should be excluded, such as small bowel bacterial overgrowth, GI infection (clostridium difficile), bile acid malabsorption, inflammatory bowel disease, microscopic colitis, lactase deficiency and other food intolerances (8). Long term follow-up of patients with PEI is recommended, considering the risk for malnutrition, including clinical, anthropometric, and biochemical measures of nutritional status, as well as bone health (2,8). Anthropometric measures include body weight, grip strength, mid-arm circumference, measurement of muscle-mass on CT scans if available, functions tests such as 6-min walk tests etc. Clinical assessment focuses on GI symptoms, QoL, compliance to treatment, and findings such as sarcopenia or oedema. Biochemical evaluation includes full blood count and usual chemistry panel, magnesium, liposoluble vitamins, calcium and phosphorus, zinc, iron studies, vitamin B12 and folic acid, glycose and HbA1c. Follow-up depends on the nature of the underlying disease; indeed, the focus for patients with palliative management is on QoL and adequate control of symptoms, whereas invasive procedures and extensive blood tests are avoided. Finally, the authors offer a useful figure illustrating a step-by-step guidance for starting and optimizing management, as well as useful tables with practical information (including less frequent causes remated to PEI, guidance for diagnosis and follow-up etc.) (8).

Another strong point of this publication is the identification of areas of uncertainty, where further research could be applied (8). More specifically, it still remains a challenge to optimize the diagnostic yield of FE1 or develop additional noninvasive and easily available tests. PEI relayed to extra pancreatic diseases is still poorly understood and largely underdiagnosed. Patient outcomes seem to improve with PERT, but high-quality data on specific groups such as patients with pancreatic cancer or receiving enteral nutrition are still lacking. Finally, data on long-term use of PERT and direct association with bone health is scarce (*Table 1*).

To summarize, the present work offers a comprehensive guide on PEI for both specialist and non-specialist HCPs including an evidence-based assessment, as well a practical approach, that will help in increasing awareness and improving patient care.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Hepatobiliary Surgery and Nutrition*. The article did not undergo external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-22-635/coif). MA reports receiving consulting fees from Olympus, Fujifilm, Ambu and honoraria from Olympus. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Keller J, Layer P. Human pancreatic exocrine response to nutrients in health and disease. Gut 2005;54 Suppl 6:vi1-28.
2. Arvanitakis M, Ockenga J, Bezmarevic M, et al. ESPEN guideline on clinical nutrition in acute and chronic pancreatitis. Clin Nutr 2020;39:612-31.
3. Sikkens EC, Cahen DL, van Eijck C, et al. Patients with exocrine insufficiency due to chronic pancreatitis are undertreated: a Dutch national survey. Pancreatology 2012;12:71-3.
4. Erchinger F, Tjora E, Nordaas IK, et al. Pancreatic enzyme treatment in chronic pancreatitis: Quality of management and adherence to guidelines-A cross-sectional observational study. United European Gastroenterol J 2022;10:844-53.
5. de la Iglesia-Garcia D, Vallejo-Senra N, Iglesias-Garcia J, et al. Increased Risk of Mortality Associated With Pancreatic Exocrine Insufficiency in Patients With Chronic Pancreatitis. J Clin Gastroenterol 2018;52:e63-72.
6. de la Iglesia-García D, Huang W, Szatmary P, et al. Efficacy of pancreatic enzyme replacement therapy in chronic pancreatitis: systematic review and meta-analysis. Gut 2017;66:1354-5.
7. Roberts KJ, Bannister CA, Schrem H. Enzyme replacement improves survival among patients with pancreatic cancer: Results of a population based study. Pancreatology 2019;19:114-21.
8. Phillips ME, Hopper AD, Leeds JS, et al. Consensus for the management of pancreatic exocrine insufficiency: UK practical guidelines. BMJ Open Gastroenterol 2021;8:e000643.
9. Zhang J, Hou J, Liu D, et al. The Prevalence and Characteristics of Exocrine Pancreatic Insufficiency in Patients with Type 2 Diabetes: A Systematic Review and Meta-Analysis. Int J Endocrinol 2022;2022:7764963.
10. Löhr JM, Dominguez-Munoz E, Rosendahl J, et al. United European Gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis (HaPanEU). United European Gastroenterol J 2017;5:153-99.

Cite this article as: Arvanitakis M, Hadefi A, Viesca MFY. Optimizing management of patients with pancreatic exocrine insufficiency. HepatoBiliary Surg Nutr 2023;12(1):128-130. doi: 10.21037/hbsn-22-635