

# Update nutritional management in patients with pancreatic ductal adenocarcinoma: A literature reviews

## Abstract

Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal malignancies. Only 20 % of patients are operable at the time of diagnosis. However, the survival rate varies among patients depending on immune response and nutritional status. Weight loss (WL) is frequent and multifactorial, so anorexia-cachexia syndrome and exocrine pancreatic insufficiency (EPI) should be considered. The nutritional care process must be carried out in all cases from the moment of suspected diagnosis and during the disease. The management of patients with PDAC must be personalized, individualizing behaviors, and from a multidisciplinary perspective at each stage of the disease.

The objective of the present review is to offer a tool that facilitates the identification of individuals at nutritional risk and to describe the most appropriate nutritional strategies to improve the quality of care for patients with PDAC.

**Keywords:** pancreatic ductal adenocarcinoma, malnutrition, nutritional therapy, exocrine pancreatic insufficiency, pancreatic enzymes replacement therapy

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Ailen Suarez,<sup>1</sup> Inés Marturano,<sup>1</sup> Rocío Sánchez Canicoba,<sup>2</sup> Marisa Canicoba<sup>1</sup>

<sup>1</sup>Department of Food and Diet Therapy, Alejandro Posadas National Hospital, Argentina

<sup>2</sup>Nutritional Support Unit, Galician Health Service, Xeral Subdirectorate, Spain

**Correspondence:** Marisa Canicoba, Department of Food and Diet Therapy, Alejandro Posadas National Hospital, Buenos Aires, Argentina, Email marisa.canicob@gmail.com

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**Abbreviations:** PDAC, pancreatic ductal adenocarcinoma; WL, weight loss; MN, malnutrition; CT, chemotherapy; EPI, exocrine pancreatic insufficiency; RT, radiotherapy; ESPEN, European Society for Clinical Nutrition and Metabolism; LOS, longer hospital stay; NT, nutritional therapy; ONS, oral nutritional supplements; EN, enteral nutrition; PN, parenteral nutrition; PERT, pancreatic enzyme replacement therapy; ERAS, Enhanced Recovery After Surgery; POPF, postoperative pancreatic fistula; CPD, cephalic pancreaticoduodenectomy, IN; immunonutrition, IU, international units.

## Introduction

Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal malignancies. Between 80-85% of patients have advanced disease at the time of diagnosis and the five-year survival rate is 10%, which varies between patients depending on the immune response and nutritional status.<sup>1-3</sup> Due to the difficulty in early diagnosis of PDAC, only 20% of patients can benefit from surgical resection.<sup>3-5</sup> malnutrition (MN) is a common feature among patients with PDAC, with approximately 80% reporting unintentional weight loss (WL) at the time of diagnosis, and more than one-third having lost more than 10% of their body weight, leading to which increases complications related to chemotherapy (CT) the postoperative period and survival.<sup>4,6-8</sup> Identifying patients at risk for MN and applying the nutritional care process may be beneficial in improving outcomes and quality of life for patients with PDAC. The objective of the present review is to offer a tool that facilitates the identification of individuals at nutritional risk and to describe the most appropriate nutritional strategies to improve the quality of care for patients with PDAC.

## Material and methods

### Study selection

A total of 258 articles that met the selection criteria identified through the Medline (Pubmed) and Cochrane Library search criteria were selected, of which 49 articles were included for this review.

All identified studies were independently examined, those that were considered of interest and that presented summary, objectives, results and conclusions on the importance of nutrition in PDAC were included, and ineligible articles were excluded.

The following search terms were used in all possible combinations: pancreatic ductal adenocarcinoma, nutritional evaluation, malnutrition, nutritional therapy, body composition, toxicity, exocrine pancreatic insufficiency, pancreatic surgery.

### Epidemiology

In 2020, worldwide, the incidence rate of PDAC was 4.9 per 100.000 population for both sexes, and the mortality rate was 4.5 per 100.000 population. There is an increasing trend worldwide in both incidence and mortality.<sup>2</sup> The Global Burden of Disease study indicated that PDAC in 2017 was the seventh cause of death from cancer and is expected to be the third cause in the coming years.<sup>9</sup> PDAC represents 90% of malignant solid tumors of this gland; The remaining 10% includes neuroendocrine and acinar tumors. In this review we refer specifically to PDAC.<sup>3</sup>

### Modifiable risk factors

The exact cause of PDAC is currently unknown, but there are modifiable risk factors such as toxic metabolic habits:

**Smoking:** the duration of the habit and the number of cigarettes per day increase the risk of developing PDAC, being almost two times higher in smokers compared to those who never smoked.<sup>1,3,5,10</sup>

**Alcohol:** consumption greater than 30 and 60 grams/day is considered a risk factor for PDAC.<sup>1</sup>

**Obesity:** is recognized as a systemic pro-inflammatory state associated with an increased risk of developing tumors in multiple organs, including the pancreas.<sup>1,3,10</sup>

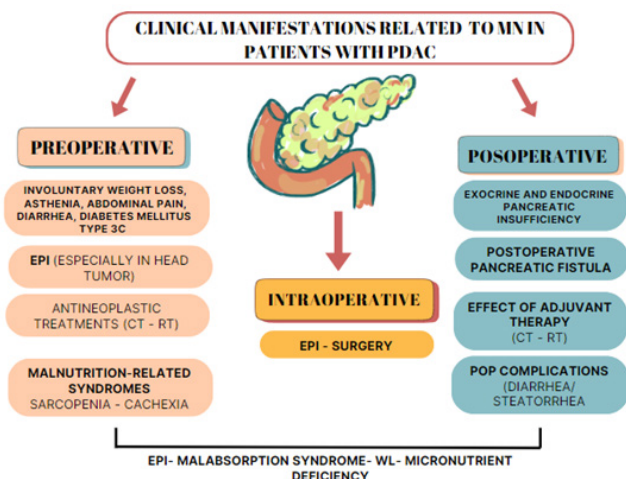
**Diabetes mellitus:** it is both a risk factor and a consequence of PDAC and also an early manifestation of it<sup>1</sup> Long-term diabetes (greater than three years) has been associated with a 1.5- to 2.4-fold increased risk of PDAC.<sup>3,5,10</sup>

**Diet:** based on ultra-processed foods, refined flours, fructose, alcohol and red meat shows a significant and consistent association with the risk of general cancer, mainly PDAC.<sup>11-13</sup>

### Clinical manifestations related to MN

Clinical manifestations include numerous and variable signs and symptoms, sometimes nonspecific, that depend on the location and extent of the disease. Patients with tumors located in the head area (70-80%) usually present symptoms earlier than those with distal tumors.

The most frequent clinical manifestations related to MN are detailed below (Figure 1).



**Figure 1** Clinical manifestations related to MN in patients with PDAC.

**Abbreviations:** EPI, exocrine pancreatic insufficiency; ERAS, Enhanced Recovery After Surgery; NJT, nasojejunal tube; PDAC, pancreatic ductal adenocarcinoma; CT, chemotherapy; RT, radiotherapy.

**Adapted:** Halle-Smith JM, Powell-Brett SF, Hall LA, et al. Recent advances in pancreatic ductal adenocarcinoma: Strategies to optimise the perioperative nutritional status in pancreatoduodenectomy patients. *Cancers (Basel)* [Internet]. 2023;15(9):2466.

- Asthenia:** observed in 86% of patients. Loss of appetite, pain, fatigue, depression, early satiety, vomiting, and malabsorption symptoms contribute to this clinical manifestation.<sup>1,7</sup>
- WL:** occurs in 80% of patients, it is an independent predictor of worse survival in patients with PDAC.<sup>1,4</sup>
- Abdominal pain:** occurs in 79% of patients, which leads to low caloric-protein intake.<sup>1</sup>
- Exocrine pancreatic insufficiency (EPI):** defined as the state of maldigestion of nutrients caused by the insufficient secretion of pancreatic enzymes and/or bicarbonate, their inadequate activation, their early degradation and/or the inefficient enzyme-food interaction, which leads to a calorie-protein MN and vitamin deficiencies.<sup>14-17</sup>

EPI can occur at the onset of the disease, after surgery as an early sequelae, or during CT in advanced stages.<sup>16,17</sup> The prevalence of EPI in cephalic PDAC is 60-70% and increases to 92% after a two-month follow-up. In other locations the prevalence is lower.<sup>14,18</sup>

- Persistent inflammation:** catabolic effects derived from the inflammatory state impact WL and sarcopenia, which are mediated by several cytokines that could be involved with cancer cachexia in patients with PDAC.<sup>17,19,20</sup>

- Diabetes Mellitus type 3c or pancreatogenic:** defined as the dysfunction and loss of pancreatic islets as a consequence of diseases of the exocrine pancreas.<sup>1</sup>

- Treatment side effect:** antineoplastic treatment such as CT and radiotherapy (RT) can significantly impact nutritional status.<sup>8</sup> 70% of patients develop MN during CT.<sup>4</sup>

- Mechanical or functional alterations of the digestive system due to pancreatic surgery:** these modifications produce changes in the digestion-absorption of nutrients, impacting the nutritional status due to delayed gastric emptying, malabsorption, EPI and hyperglycemia. Additionally, the ability to consume adequate oral intake after surgery does not recover quickly.<sup>17</sup>

### Syndromes related to MN

Patients may present to surgery with a variety of syndromes and underlying nutritional phenotypes including:

- Cancer cachexia:** occurs in approximately 70-80% of patients with PDAC and contributes to 33% of mortality.<sup>20</sup> The risk of progression through the stages of cachexia depends on factors such as: type of cancer, stage, food intake, presence of systemic inflammation, inactivity, lack of response or complications to systemic anticancer therapies, and /or the aftermath of surgery.<sup>21</sup>
- Sarcopenia:** it is an independent risk factor for pre- and postoperative complications, the prevalence ranges between 30% and 65%.<sup>22</sup> It is associated with toxicity induced by CT.<sup>6,23</sup>
- A systematic review by Ratnayake et al.<sup>24</sup> and recently, a meta-analysis carried out by Thormann et al.<sup>23</sup> concluded that sarcopenia was not correlated with postoperative complications, but was associated with longer hospital stay (LOS).
- Sarcopenic obesity:** demonstrated to have an impact on surgical complications, overall survival, was associated with surgical complications and CT toxicity, and earlier disease recurrence in patients with PDAC.<sup>6,17,25</sup>

### Nutritional care process

Nutritional care should be considered as a continuous and binding process that consists of three stages: detect, nourish and monitor and in five steps: screening, evaluation, diagnosis and nutritional intervention, monitoring and continuity of treatment upon hospital discharge.<sup>26</sup>

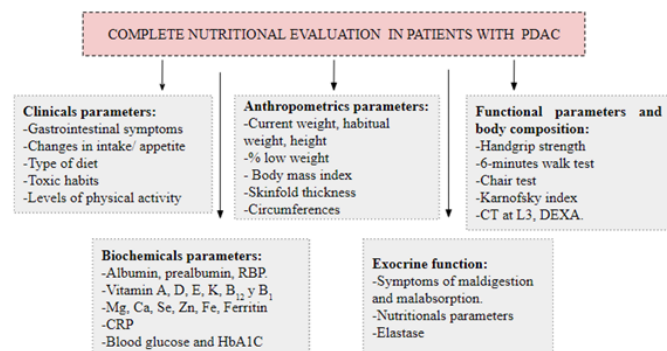
### Risk detection and nutritional evaluation

Early detection and assessment of nutritional status are vital to identify patients at risk for MN, optimize preparation for surgery, minimize perioperative risks, and offer better postoperative recovery.<sup>27</sup>

It should be carried out from the first consultation and periodically during the different phases of the treatment of the disease.<sup>1,4,10,27,28</sup>

Tools have been developed and validated to identify the risk of MN in oncology patients, which allow the identification and referral of patients at nutritional risk to a nutritionist for a complete nutritional evaluation.<sup>1,4,28</sup> The gold standard tool to evaluate the nutritional status of oncology patients is the subjective global assessment generated by the patient that can be used in the context of preoperative evaluation. However, more studies must be conducted to use it in patients with PDAC.<sup>1,29</sup> The detection of MN through the global leadership initiative on malnutrition criteria has a negative impact on overall survival and an increase in postoperative complications in cancer patients.<sup>30-32</sup>

To complete the nutritional evaluation, the following parameters must be considered: clinical, anthropometric, functional, biochemical, dietary intake and exocrine function (Figure 2).

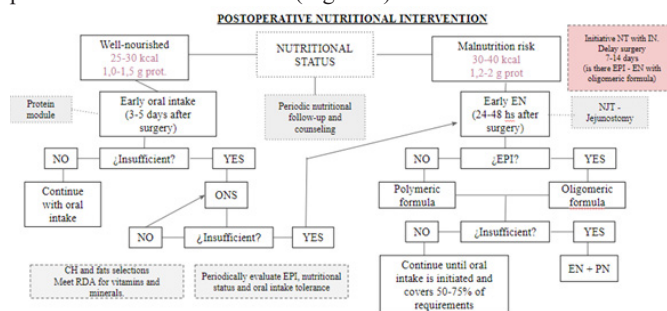


**Figure 2** Complete nutritional evaluation in patients with PDAC.

**Abbreviations:** CRP, C-reactive protein; CT, computed tomography; DEXA, dual energy x-ray absorptiometry; HbA1C, glycosylated hemoglobin; L3, lumbar three; PDAC, pancreatic ductal adenocarcinoma; RBP, Retinol Binding Protein.

## Nutritional intervention

Nutritional requirements should be established based on the patient's nutritional demands (Figure 3).



**Figure 3** Postoperative nutritional intervention.

**Abbreviations:** CH, carbohydrates; EN, enteral nutrition; EPI, exocrine pancreatic insufficiency; IN, immunonutrition; NJT, nasojejunal tube; NT, nutritional therapy; ONS, oral nutritional supplements; PN, parenteral nutrition; RDA, recommended dietary allowances.

According to the guideline of the European Society for Clinical Nutrition and Metabolism (ESPEN)<sup>33</sup> for cancer patients, consider a contribution of 25-30 kcal/kg/day. In patients MN of 30-40 kcal/kg/day. Regarding protein intake, an intake of more than 1.0-1.5 g/kg/day and at least 1.2 to 2 g/kg/day to balance protein synthesis.<sup>1,20,28,34</sup> Regarding carbohydrates and fats should not be restricted, but an individualized selection should be made.<sup>1</sup> On the other hand, it is recommended to cover micronutrients as established by the Recommended Dietary Allowance and supplement in case of deficiency.<sup>1,33,34</sup>

Individualized nutritional counseling has become a standard of recommendation by ESPEN, subsequently suggested by the European Society for Medical Oncology, and the Spanish Society of Medical Oncology. This modality reduces the toxicity of the treatment, improves intake and nutritional status, as well as the patient's quality of life.<sup>10,28,33,35</sup>

## Nutritional therapy in patients with PDAC

Nutritional therapy (NT) consists of the provision of nutrients to patients who cannot meet nutritional requirements or do not tolerate

the oral route. Its main goal is to prevent or treat MN. NT can be initiated with oral nutritional supplements (ONS), enteral nutrition (EN) and exclusive or complementary parenteral nutrition (PN), which should be considered only in cases where oral route or EN is not feasible or tolerated.<sup>1,33,36</sup>

The benefit of NT is obtained when it is indicated to the right patient and at the right time.<sup>33,37</sup>

## Pancreatic surgery

Pancreatic surgery has always been challenging due to the anatomical complexity of the pancreas. Alteration in the secretion of pancreatic enzymes determines a series of gastrointestinal symptoms with abdominal pain, abdominal distension, delayed gastric emptying, diarrhea, lack of appetite, nausea, dyspepsia, malabsorption and consequently WL and EPI.

The patient's performance status, comorbidities and nutritional status will be the main determinants of therapeutic decisions

For nutritional purposes, the following clinical scenarios will be considered:<sup>4</sup>

**i. Potentially resectable tumor/borderline tumor:** represents 20% of PDAC. Although surgery is the first-line therapy in resectable tumors, neoadjuvant CT and/or RT may be considered prior to surgery. It is recommended before and during antineoplastic treatment to perform a nutritional evaluation and intervention due to the symptoms that patients may present and that may have an impact on nutritional status.

**ii. Locally advanced tumor:** represents 30% of cases. The standard of care is CT, and RT with side effects leading to dose reduction, delays, or discontinuation of treatment. It is essential to evaluate the nutritional status of these patients to limit its impact on increased side effects and treatment interruption.

**iii. Metastatic disease:** accounts for 50% of PDAC. More than 80% suffer significant WL at the time of diagnosis and over time develop cachexia, recognized as one of the main causes of decreased quality of life, survival, and treatment failure.

## Nutritional strategies in the preoperative

In recent years, there has been discussion about the benefits of nutrients in the preoperative phase.<sup>33</sup> ESPEN<sup>33</sup> for cancer patients recommends, in those who are MN or at risk of being so and in those who can eat food, to provide nutritional advice, information on the treatment of symptoms and disorders that prevent adequate food intake and, if necessary, offer them ONS. Patients with cancer in the head of the unresected pancreas are at risk for EPI, preoperative incidence is challenging, difficult to evaluate, and there is no ideal diagnostic test. Therefore, pancreatic enzyme replacement therapy (PERT) should be considered for all patients with a malignant tumor of the head of the pancreas awaiting resection.<sup>1,6</sup>

## Prehabilitation programs

Are defined as any intervention aimed at improving the patient's health and lifestyle before definitive therapy, usually surgery. Evidence has focused on three main elements: exercise and preconditioning, nutrition, and psychological well-being that may contribute to decreasing postoperative complication rates and shortening the duration of LOS in patients undergoing major abdominal surgery.<sup>36,38,39</sup>

### In patients undergoing pancreatic resection this strategy may have potential benefits:

- Firstly, transform unfit patients with a high risk of perioperative mortality into surgical candidates.
- Secondly, improve results in patients considered suitable for major surgery.

Prehabilitation may improve outcomes after pancreatic surgery, but there is currently a lack of standardization with programs varying in content and duration.<sup>40</sup>

### Intraoperative nutritional strategies

In the current surgical environment, cancer patients undergoing surgery should be managed within the Enhanced Recovery After Surgery program (ERAS)<sup>39</sup> that seeks to minimize surgical stress, maintain nutritional status, reduce complications, and optimize recovery rate and duration. of the LOS. This program includes the reduction of preoperative fasting (6 hours for solids and 2 hours for liquids) before anesthetic induction and oral carbohydrate loading 2 hours before the intervention in non-diabetic patients. Although these recommendations are not specific to pancreatic surgery patients, the beneficial effect of this simple intervention would be valuable in this population known to have a significant risk of perioperative MN.

However, due to EPI, all patients should be screened for diabetes before loading carbohydrate drinks to prevent hyperglycemia.<sup>39</sup>

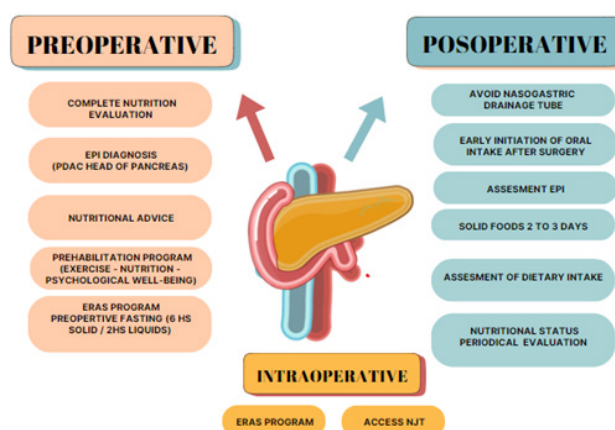
In MN patients, placement of a nasojejunal tube should be considered in all those who will undergo pancreatic surgery.<sup>36</sup>

The ERAS guidelines<sup>39</sup> for pancreatic surgeries indicate that patients should be allowed unrestricted eating after surgery, but patients should be advised to increase intake every three to four days to improve tolerance.

### Nutritional strategies in the postoperative period

It is recommended to perform a periodic reevaluation of nutritional status after surgery (Figure 4). The routine use of a nasogastric drainage tube should be avoided.<sup>4,6,40,41</sup> Traditionally, early oral diet administration (24 hours) after pancreatic surgery has been avoided, probably for fear of stimulating the pancreatic remnant or mechanical injury, which could increase the risk of postoperative pancreatic fistula (POPF). However, administering orally early after surgery is a safe practice and is associated with decreased LOS duration. There is no difference in complications, delayed gastric emptying and mortality compared to EN. Solid foods can be started between the second and third day. At this stage the protein objective is important, progressing to a complete, varied diet, divided into five to six meals and reduced volume (Figure 4).<sup>6</sup> The start of EN within the first 24-48 hours will be indicated as the first option in patients who cannot start early oral diet, and in those who cannot cover 50% of nutritional requirements. The access route for EN can be nasojejunal. or feeding jejunostomy. The choice will depend on the treating team.<sup>1,6</sup> PN will be indicated when other feeding routes are not feasible or when it is necessary to implement it in a complementary manner in patients who cannot meet nutritional requirements through other means.<sup>1</sup>

Adiamah et al.<sup>42</sup> conducted a review in 690 patients (EN= 383 and PN= 307) that included 5 randomized controlled trials and demonstrated that EN was associated with lower LOS compared to PN in patients undergoing cephalic pancreaticoduodenectomy (CPD). ERAS<sup>39</sup> for pancreatic surgeries indicate that patients should be allowed unrestricted eating after surgery, but they should be advised to increase intake every three to four days to improve tolerance.



**Figure 4** Nutritional strategies in the perioperative period to optimize nutritional status in patients with PDAC.

**Abbreviations:** CT, chemotherapy; EPI, exocrine pancreatic insufficiency; MN, malnutrition; PDAC, pancreatic ductal adenocarcinoma; RT, radiotherapy; WL, weight loss; ERAS, Enhanced Recovery After Surgery; NJT, nasojejunal.

**Adapted:** Halle-Smith JM, Powell-Brett SF, Hall LA, et al. Recent advances in pancreatic ductal adenocarcinoma: Strategies to optimise the perioperative nutritional status in pancreatoduodenectomy patients. *Cancers (Basel) [Internet]*. 2023;15(9):2466.

### Immunonutrition

Immunonutrition (IN) through formulas enriched with arginine, omega-3 fatty acids and/or ribonucleic acid, can be administered orally or via EN in the preoperative or postoperative setting in patients with CPD (Figure 4). One of the most important studies of the role of IN in CPD is that of De Luca et al.<sup>43</sup> in a randomized trial of 212 patients who were going to undergo CPD, they were distributed into three groups: standard isocaloric EN (n=73 patients), EN formula enriched with IN (n=71 patients) and NP (n=68 patients). The IN formula group presented a significant improvement in their immunometabolism response, fewer postoperative complications, and a shorter LOS compared to the other two alternatives.

In a meta-analysis carried out by Guan et al.<sup>44</sup> in patients undergoing CPD, they suggest the use of formulas enriched with IN and highlight the need for more well-designed randomized clinical trials with sufficient statistical power. Another systematic review and meta-analysis published by Fan et al.<sup>45</sup> involving 10 studies (572 patients) demonstrated that the use of IN significantly reduced LOS in patients with pancreatic cancer, Mean Deviation = -2.31; 95% CI = -4.43; -0.18; P = 0.03) with low heterogeneity. Furthermore, the incidence of infectious complications was significantly reduced (Mean Deviation = 0.42, 95% CI = 0.18, 1.00, P = 0.05). For surgical patients in general, ESPEN<sup>36</sup> recommends the peri- or at least post-operative administration of specific formulas, enriched with arginine, omega-3 fatty acids and ribonucleotides in MN patients who will undergo major oncological surgery. On the other hand, it suggests the administration of ONS with IN five to seven days before surgery to MN or at-risk patients who are going to undergo major abdominal surgery. Although it mentions that there is currently no clear evidence on the exclusive use of formulas with IN versus standard formulas in the preoperative period in isolation. The benefit of IN in the perioperative period derives from the synergistic effect of the three main immunonutrients (arginine, nucleotides and omega 3).<sup>1</sup> On the other hand, the ERAS regarding pancreatic surgery indicate that there is little evidence to recommend IN in these patients.<sup>41</sup>

## Nutritional strategies during CT and RT

It is recommended during RT to ensure adequate nutritional intake mainly through individualized nutritional counseling and/or with the use of ONS, in order to avoid MN, maintain intake and avoid interruptions of RT.<sup>33</sup> If orally is inadequate, EN is preferable to PN unless there is severe mucositis.<sup>33</sup> Routine PN is not indicated during RT, only if adequate oral and/or EN support is not available (for example, severe radiation enteritis or severe malabsorption).<sup>33</sup> During intensive CT, it is recommended to maintain physical activity and ensure adequate nutritional intake.<sup>33</sup> There is not enough consistent clinical data to recommend glutamine to prevent RT induced enteritis/diarrhea, stomatitis, esophagitis, or skin toxicity, or to recommend probiotics to reduce RT induced diarrhea.<sup>33</sup> At the same time, neutropenic diets are not recommended to prevent infections in cancer patients during active treatment of CT.<sup>33,46</sup>

### Physical exercise

The American Society of Clinical Oncology<sup>35,47</sup> recommends that patients perform regular aerobic and resistance exercise during active cancer treatment with curative intent to mitigate its side effects.

### Post-surgical complications:

Partial or total resection of the pancreas can lead to EPI or endocrine insufficiency. Regarding EPI, the decrease in the amount of pancreatic secretions is responsible for diarrhea (with or without steatorrhea) which can be prevented with PERT, nutritional advice and antidiarrheal medications that are sometimes necessary to improve the patient's quality of life.

### The most frequent complications are the following:

- **POPF:** it is one of the most common and serious complications after surgery leading to worse nutritional outcomes and contributing to higher postoperative morbidity and mortality. The International Study Group on Pancreatic Fistula<sup>6</sup> in 2016 redefined it as an abnormal communication between the pancreatic ductal epithelium and another epithelial surface that contains fluid rich in enzymes derived from the pancreas with a level of amylase in the drainage (not the blood value) three times higher than the normal value, becoming the main diagnostic indicator of POPF.

According to the group,<sup>6</sup> stable patients with a type A (currently called "biochemical leak") or type B fistula can tolerate oral feeding. However, each case must be approached particular. Type C leads to organic failure possibly requiring surgery and/or morbidity or even death. Therefore, patients who are at high risk for POPF may benefit from NT through a nasojejunal tube that can be placed during surgery.<sup>1,6</sup>

- **EPI:** is another of the postoperative complications of PDAC and justifies the use of PERT in those patients who present signs of malabsorption.

### Treatment of EPI

EPI treatment aims to achieve correct digestion-absorption of food, control symptoms and improve the nutritional status of patients.<sup>18,48,49</sup> It consists of the indication of PERT along with individualized nutritional advice. It begins with a low dose of enzymes, considering the individual's eating pattern, and is subsequently increased depending on the fat content of the diet, the characteristics of the stool, improvement in nutritional parameters and gastrointestinal symptoms.

## TREP consumption

It refers to the oral administration of capsules containing commercially produced digestive enzymes namely: lipase, protease and amylase. An initial dose of 40.000 to 50.000 international units (IU) of lipase is suggested with main meals, and half that dose with minor meals. This dose may be insufficient in patients with pancreatic head tumor, who may require a dose of 75.000 IU per meal. All guidelines support increasing the dose if the initial dose is not effective.<sup>14,15,37</sup> Enzymes should be consumed during meals and swallowed intact, without crushing or chewing. For long meals it may be beneficial to take part of the enzyme dose in the first bite and then distribute them throughout the meal.<sup>14,15,37</sup> Supplementation with fat-soluble and water-soluble vitamins and micronutrients should be considered in patients with low plasma concentrations.<sup>14,15,37,49</sup>

### Diet plan in patients with EPI

The eating plan must be individualized, healthy and without fat restriction; a low-fat diet can exacerbate MN.<sup>15</sup> Patients with MN require frequent, small intakes of proteins of high biological value. Do not exceed the consumption of 30 grams of fiber daily.<sup>14,18,48</sup>

The suspension of toxic habits must be achieved. Patient follow-up should be accompanied by periodic evaluation by a nutritionist to determine the NT requirement.<sup>14,37</sup>

### EN and EPI

Administration of TREP via the EN formulation is not supported by guidelines, results in increased manipulation, and may even clog the feeding tube. Furthermore, there are no studies that demonstrate the effectiveness or safety of this practice.<sup>1,18</sup>

### Exclusive EN

It is recommended to use oligomeric or semi-elemental formulas, which contain medium chain triglycerides, which do not require pancreatic lipase for absorption. If the patient can ingest the capsules, an alternative may be to administer them orally: one dose at the beginning of EN with a polymeric formula, another in the middle and another at the end of the intermittent infusion.<sup>1,18</sup>

### Complementary EN + oral ingestion:

It is recommended to use oligomeric or semi-elemental formulas for cyclic EN (for example, nocturnal), and TREP can be consumed orally, depending on the diet of each patient. If the patient can ingest the capsules, an alternative may be distributed administration: one dose at the beginning of EN, in the middle and another at the end of the intermittent infusion of a polymeric enteral formula.<sup>1,18</sup>

### TN in advanced cancer

The benefit of NT must be carefully considered. If the expected survival is greater than three months or years, NT should be administered with the objective of administering adequate energy and protein intake, reducing metabolic alterations, and maintaining an adequate functional status and subjective quality of life.<sup>28</sup>

If expected survival is in the range of a few to several weeks, interventions should be non-invasive.

ESPEN<sup>33</sup> suggests that for patients with advanced cancer undergoing CT and at risk of WL or MN, use long-chain omega-3 fatty acids or fish oil to stabilize or improve appetite, food intake, and lean body mass and body weight.

## Conclusion

MN is a common feature among patients with PDAC, which increases treatment-related complications. It is important to optimize strategies to provide adequate nutrition at the right time, which reduces the toxicity of the treatment, improves intake and nutritional status, as well as the patient's quality of life.

The management of the patient with PDAC must be personalized, and from a multidisciplinary perspective.

Future research in this population should focus on: understanding physiological mechanisms underlying nutritional therapies, such as immunonutrition and probiotics, improving the diagnosis of exocrine pancreatic insufficiency, and developing robust clinical trials that can evaluate the efficacy of these different nutritional strategies.

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## Conflicts of interests

The authors declare no conflict of interest.

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