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Preoperative and Postoperative Nutritional Support Methods For Pancreatic Cancer: A Review

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Abstract:

Pancreatic cancer (PC) is a highly malignant neoplasm often detected at an advanced stage, resulting in a poor prognosis. Major risk factors include cigarette smoking, excessive alcohol consumption, obesity, and genetic predisposition. Malnutrition, cachexia, and sarcopenia are prevalent among PC patients and significantly impact clinical outcomes. Evidence suggests that perioperative nutritional interventions—ranging from early screening and assessment to oral supplementation, pancreatic enzyme replacement therapy, and enteral or parenteral nutrition—can alleviate postoperative complications, shorten hospital stays, and enhance quality of life. Early refeeding and stepwise dietary advancement are vital to maintaining gastrointestinal function and meeting energy requirements. In addition, continuing patient education and home-based nutritional management after discharge are crucial, as many patients remain at high risk of nutritional deficits postoperatively. Despite these benefits, standardized disease-specific guidelines for nutritional support in PC are still lacking, and further investigation is required to determine optimal strategies and timing for interventions. Multidisciplinary collaboration, involving surgeons, oncologists, and dietitians, is essential for addressing the multifaceted nutritional challenges encountered by PC patients and for improving both survival and quality of life. Future research should also focus on refining assessment tools, identifying specific biomarkers, and evaluating long-term outcomes to establish more targeted nutritional guidelines for PC care.

Keywords: Pancreatic cancer; Malnutrition; Perioperative management; Nutritional intervention; Cachexia

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1. Introduction

Pancreatic cancer (PC) was the cause of 467,005 deaths in 2022 alone, accounting for 4.8% of cancer mortality in 185 countries and ranked sixth out of 36 types of cancer [1]. It is a malignant, invasive tumor with a high risk of mortality, and, though generally more prevalent in men and adults aged 60-85, is increasingly observed in younger populations [2]. RSP has few early symptoms and is often diagnosed at an advanced stage, leading to a poor 5-year survival rate of only 2-9% [3], with mortality rate increasing with age [4]. Many factors have been associated with the occurrence of PC, such as smoking, alcohol, and obesity [3]. However, the specific nutritional approaches in PC therapy and post-operation care remain a field worthy of exploration, as 70.3% of PC patients experience malnutrition during PC chemotherapy, which leads to shorter survival time, reduced quality of life (QOL), and a higher chance of chemotoxicity during treatment [5]. Moreover, studies have shown that the nutritional and inflammatory conditions of patients perioperatively and during chemotherapy do affect future oncological outcomes [6]. PC often leads to Pancreatic exocrine deficiency, a decrease in the production of pancreatic enzymes and bicarbonates which impairs digestive functions, a leading cause of malnutrition in PC patients [7]. This review aims to outline recent advances and case studies of nutritional support in PC treatment and conclude the most common problems and solutions faced. It will explore the interplay between nutritional strategies and therapeutic outcomes, highlighting the role of tailored nutritional interventions in improving patient prognosis and quality of life.

2. Risk factors

2.1 Family History and Genetic Factors

There has been a major positive correlation observed between family PC history and risk of PC in patients, specifically, a twofold increase of risk in individuals with a single diagnosed family member compared with the general population, and a sevenfold increase in individuals with multiple diagnosed family members. Several high-risk PC susceptibility genes have been identified, including BRCA1, BRCA2, and ATM. Testing for PC susceptibility gene variants is one way of recognizing increased inherited risks in individuals, and, the method of surveilling and testing carriers with susceptibility genes and family history could be used to diagnose early and significantly lower PC mortality [8].

2.2 Cigarette and alcohol use

Cigarette smoking is an established cause of PC, with a 1.7-fold increase in risk in smokers as opposed to non-smokers [8], and a positive correlation between the number of cigarettes consumed and risk of Pc, with an odds ratio (OR) of 3.4 in those who smoke ≥35 cigarettes per day [9]. However, studies have shown that risk is reduced as elapsed time increases since cigarette cessation, decreasing to OR=0.98 after 20 years of quitting. In addition, there has also been a positive correlation observed between lifetime alcohol consumption and PC risk, with a 1.6-fold increase in risk in those who consume >6 drinks per day compared to those who consume >1 drink per day [8]. There was a stronger association observed in men, and the consumption of spirits, liquor, and beer appeared to pose more risk [10]. These findings highlight the critical role of modifiable lifestyle factors, such as smoking and alcohol consumption, in influencing pancreatic cancer risk, underscoring the importance of preventive measures and lifestyle interventions in reducing disease burden.

2.3 Diabetes and Body Mass Index (BMI)

Long-term diabetes (>2 years) has been associated with a 1.6-fold increase in PC risk, while all diabetes have been observed to have a 1.8-fold increase [11]. 80% of PC patients have glucose intolerance or frank diabetes [12]. The symptoms of reduced glucose tolerance, insulin resistance, and hyperinsulinemia in adult diabetes also strongly relate to the physiological consequences of excess adiposity [16], bringing into question the relationship between obesity and PC. Obesity has been established as a modifiable risk factor across different cancers [13]. However, though cohort studies generally support obesity, measured by Body Mass Index (BMI) or waist-hip ratio (WHR), as an independent risk factor of PC, discrepancies exist across studies and study locations [14]. In a population study of 900,000 adults, the mortality rates of male cancer patients with BMI >40 kg/m^2 compared to normal weight increased by 52%, while in female patients it increased by 62% [15]. Though not specific to PC, this study displays a significant correlation between obesity and cancer mortality.

2.4 Age

Though the global incidence of PC in younger patients has been rising, age is still an established risk factor [16]. Most cases occur later in life, with the global peak being between 65 and 79 years old [17]. However, for this reason, many younger patients are diagnosed in a more advanced stage as PC isn't commonly considered.

3. Nutritional Risk Factors in PC Patients

3.1 Pre-operative Malnutrition Factors

Due to the insidious symptoms of early-stage pancreatic cancer, patients often experience persistent nutritional depletion. Approximately 85% of patients exhibit weight loss at the time of diagnosis [18], and nearly 80% suffer from cancer-related malnutrition [19]. The contributing factors include:

3.1.1 Insufficient Intake.

Nearly 50% of patients with resectable pancreatic cancer consume less than 75% of their daily caloric needs [19]. Research indicates that multiple factors lead to reduced food intake in these patients, such as tumor-secreted factors (Dilp8, Upd2) [20] and pro-inflammatory cytokines (tumor necrosis factor-α, interleukin-1) [21], which disrupt appetite regulation; discomfort caused by indigestion, chronic cancer pain, etc.; and psychological disorders like anxiety, fear, and depression, leading to subjective anorexia.

3.1.2 Absorption Impairment.

Patients with pancreatic cancer often experience significant skeletal muscle loss due to cachexia. Studies have shown that early tissue depletion is associated with pancreatic exocrine insufficiency (PEI) [22]. The main mechanisms of PEI include obstruction of the main pancreatic duct, glandular fibrosis, and a reduction in exocrine cell mass, leading to decreased or asynchronous secretion of pancreatic enzymes [23]. PEI-related nutritional absorption disorders may be accompanied by symptoms such as diarrhea and steatorrhea. Tumor invasion can impair the function of adjacent organs, and obstructive jaundice disrupts enterohepatic circulation, resulting in poor lipid absorption. Digestive tract obstruction may lead to imbalanced internal homeostasis.

3.1.3 Increased Consumption and Metabolic Disorders.

Resting energy expenditure (REE) is elevated in pancreatic cancer patients [24]. However, the feedback mechanism between REE and food intake is inadequate, resulting in a negative energy balance due to insufficient caloric intake [25]. A lower respiratory quotient indicates changes in the body's energy substrates, with increased fatty acid oxidation and amino acid gluconeogenesis, along with decreased protein synthesis [26]. Additionally, for patients undergoing neoadjuvant therapy (NAT) to achieve curative resection, the risk of nutritional deterioration due to adverse effects of chemotherapy must be considered preoperatively [27].

3.2 Post-operative Malnutrition Factors

The primary causes of elevated short-term malnutrition risk after surgery are increased demand and metabolic changes. Following resection of the primary tumor and surrounding tissues, pancreaticoduodenectomy (PD) involves digestive tract reconstruction, requiring sufficient energy and substrate supply for recovery. Anatomical and physiological changes caused by surgery result in short-term nutrient absorption disorders, increased incidence of PEI, and glucose metabolism dysregulation compared to preoperative levels [28]. Postoperative trauma and stress induce heightened catabolism, manifesting as hyperglycemia, increased energy expenditure, and enhanced protein breakdown. Postoperative complications are another critical factor leading to malnutrition. These include pancreatic fistula, biliary fistula, chylous leakage, postoperative hemorrhage, abdominal infection, and delayed gastric emptying (DGE). The clinical manifestations and severity of these complications are highly variable, increasing the risk of malnutrition. Understanding the factors affecting the nutritional status of pancreatic cancer patients during the perioperative period is essential for developing targeted nutritional treatment strategies.

4. ESPEN guidelines on nutritional support in cancer patients: the 3-step approach

4.1 Screening

The goal of early screening is to identify nutritional and metabolic disturbances early on by regularly monitoring changes in intake, weight, and BMI changes, utilizing validated tools such as Nutrition Risk Screening 2002 (NRS-2002) [29]. Screening is recommended to be conducted with all PC patients [30]. Cachexia, weight loss, and malnutrition are common nutritional concerns observed in PC patients, which is why monitoring these factors aids in the screening process [31]. Early screening aims to identify individuals at risk of malnutrition during cancer treatment efficiently, and should be affordable, highly sensitive, and specific; however, screening itself isn't sufficient to design unique treatments and nutritional pathways, and further assessment is necessary [29]. Early screening is a critical step in identifying nutritional risks in pancreatic cancer (PC) patients, but it must be followed by comprehensive assessments to develop personalized nutritional interventions.

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4.2 Assessment

In patients displaying abnormal screening results, a series of objective assessments of their nutritional intake, nutrition impact symptoms, muscle mass, physical performance, and systemic inflammation should be conducted [29]. There exist multiple nutrition and inflammatory assessment tools that could potentially be used in PC treatments, including the Glasgow Prognostic Score (GPS), Modified Glasgow Prognostic Score (mGPS), Neutrophil to Lymphocyte Ratio (NLR), and Prognostic Nutritional Index (PNI) [6]. However, these tools require further study to determine the optimal cutoff value before their clinical application [6]. Abnormal screening results in PC patients should be followed by detailed assessments using various tools, but further research is needed to establish optimal cutoff values for their clinical use.

4.3 Intervention

There remains more research and data to confirm the specific time at which nutritional intervention should begin. Still, most agree that treatment should ensue before patients are severely malnourished, as malnutrition is difficult to regress, especially in patients with deranged metabolism [29]. This is especially significant in patients with PC, as it is known that PC has an overall poor prognosis, a 5-year survival rate of 9%, and frequent occurrence of cachexia in patients [32]. The weight loss and sarcopenia that occur as a result of malnutrition could also hinder the efficacy of treatment outcomes [33].

Several forms of nutrition support may be used to treat cases of malnutrition in PC patients. To begin, nutrition counseling (nutrition history, diagnosis, therapy) conducted by licensed professionals motivates patients to increase their intake of energy-rich foods, which can improve their nutritional status and symptoms [29]. This could be achieved through adjusting meal frequencies, textural and nutritional modification of food, prescription of oral supplements, and other methods [29]. If nutrition counseling is proven to be ineffective, and patients consume significantly less than the nutritional requirements, artificial nutrition may be used [29]. Artificial nutrition includes enteral nutrition and parenteral nutrition [30]. Enteral nutrition preserves the functions of the digestive system, and is conducted by installing a nasogastric tube or feeding tube through percutaneous endoscopic gastrostomy [30]. However, when enteral nutrition through the GI tract cannot suffice for nutritional needs or if the patient's gut cannot absorb nutrition [31], parenteral nutrition, the method of injecting IV solutions containing vital nutrients directly to the bloodstream, bypassing the patient's GI tract [34]. Malnutrition remains a critical challenge in managing pancreatic cancer (PC) patients due to its association with cachexia, weight loss, and sarcopenia, which adversely impact treatment efficacy and overall prognosis. Early nutritional intervention is vital to mitigate these effects, but further research is needed to determine the optimal timing for initiating these strategies. In conclusion, addressing malnutrition in PC patients through tailored nutritional counseling and artificial nutrition methods is essential to improving their quality of life and clinical outcomes. Future studies should focus on identifying precise biomarkers and intervention windows to enhance the efficacy of nutritional support. This could lead to more personalized and effective strategies for managing malnutrition and its systemic impacts on PC care. Early and personalized nutritional interventions are crucial for managing malnutrition in pancreatic cancer patients, as they can help mitigate the detrimental effects of cachexia, weight loss, and sarcopenia, ultimately improving both treatment outcomes and overall survival.

5. Pre-operative Nutrition Support

Pre-operative malnutrition in PC patients is negatively correlated with anorexia-cachexia-associated quality of life [35]. In an investigation of postoperative outcomes between malnutrition and no-malnutrition groups, it was found that the average length of hospital stay and postoperative complication rate are both significantly higher in malnourished PC patients; through multivariate analysis, the study concludes that preoperative malnutrition is a predictor of postoperative complications [36]. Thus, preoperative nutrition support for malnourished patients before surgery proves to be valuable for their postoperative outcomes and overall quality of life.

Compared to other upper gastrointestinal (UGI) cancers such as oesophageal and gastric cancer, PC patients are less likely to receive preoperative dietetic intervention and nutritional support, despite the occurrence of malnutrition and recommendations by the ESPEN guide [37]. Patients provided with preoperative oral nutritional supplements and dietetic care reported improved preoperative weight loss, a factor linked to shorter survival in cancer patients, as well as reduced complications [37].

It is recommended for preoperative nutritional support to follow the progressive steps from oral feeding to oral nutrition supplements, enteral nutrition, and lastly parenteral nutrition [38]. Dietetics care such as nutrition counseling could be implemented in patients experiencing malnutrition preoperatively and has shown positive impacts in reducing postoperative weight loss and complications [32]. In terms of oral nutrition supplements, the intake of a fish oil-enriched conventional supplement has been found to positively impact performance and appetite in patients,

potentially helping to reverse cases of cachexia in patients with severe PC [39]. Eicosapentaenoic acid (EPA), an omega-3 fatty acid found in fish oil, had previously been found to help stabilize weight in patients with advanced PC [39]. Additionally, pancreatic enzyme replacement therapy, in which digestive enzymes are administered through oral supplements to replace pancreatic enzymes, could be used when pancreas functions are impaired due to PC [40].

6. Postoperative Nutrition Support

6.1 Comprehensive Nutritional Management and Postoperative Nutritional Support Strategy

Radical surgery for pancreatic cancer typically involves pancreaticoduodenectomy, which necessitates the resection and reconstruction of multiple biliary and gastrointestinal structures. Although the Enhanced Recovery After Surgery (ERAS) concept has significantly shortened the length of hospital stay for patients undergoing such procedures, these patients continue to face substantial tumor-related malnutrition risks and surgery-induced nutritional deficits following discharge, requiring prolonged at-home nutritional rehabilitation [38]. Studies indicate that early interventions with parenteral and enteral nutrition can improve patients' nutritional status, accelerate wound healing, reduce abdominal distension and gastrointestinal anastomotic leakage, and preserve gastrointestinal function, thereby lowering postoperative mortality to some extent [39-42]. Furthermore, individualized dietary management can significantly increase serum total protein levels and reduce complications such as intestinal obstruction and reflux esophagitis [39-42]. However, most existing nutritional management programs are concentrated in the perioperative period, with insufficient supervision following discharge. This shortcoming may exacerbate patients' nutritional deterioration [38]. Therefore, ongoing nutritional management beyond the perioperative period is crucial for enhancing clinical outcomes, shortening hospital stays, and reducing healthcare costs [38].

As a result, a holistic nutrition management model has gained increasing attention and has shown positive outcomes in conditions such as stroke, esophageal cancer, and enterostomy [43-46]. In the context of pancreatic cancer, this model emphasizes comprehensive nutritional monitoring and intervention from hospital admission to discharge and throughout home rehabilitation, encompassing nutritional screening, assessment, intervention, and follow-up [43-46]. Given that patients remain at high risk of malnutrition after radical pancreatic surgery—especially once discharged—it is recommended that they maintain a high-protein, high-energy diet, along with individualized nutritional counseling for at least 12 weeks post-discharge to mitigate the risk of malnutrition [39-42,43-46].

Under the guidance of the European Society for Clinical Nutrition and Metabolism (ESPEN) and the International Association for Surgical Metabolism and Nutrition (IASMEN), postoperative nutritional management after pancreaticoduodenectomy can be summarized as follows [46,47]:

1. Early Oral Intake and Preference for Enteral Nutrition

Whenever feasible, patients should resume oral intake as early as tolerated, gradually increasing the amount of food consumed to facilitate the recovery of gastrointestinal function, reduce the risk of complications (e.g., pneumonia), and shorten hospital stays [47,48]. If oral intake remains insufficient or poorly tolerated, enteral nutrition should be initiated promptly. Parenteral nutrition should only be considered when enteral routes fail to provide adequate nutritional support [48,51].

2. Pancreatic Enzyme Replacement Therapy

Patients who experience steatorrhea and micronutrient deficiencies due to pancreatic exocrine insufficiency should receive pancreatic enzyme replacement therapy (at least 40,000 IU per meal). Granules can be removed from capsules and mixed with food to facilitate consumption; if symptoms persist, the dosage should be adjusted accordingly [49,50]. Persistent steatorrhea necessitates investigating small intestinal bacterial overgrowth or other malabsorption causes [50].

3. Oral Supplements and Micronutrient Supplementation

Postoperative pancreatic cancer patients frequently exhibit long-term micronutrient deficiencies, particularly vitamin D, B1, B6, and iron—deficiencies in vitamin D and iron alone have been observed in over 50% of patients [52]. Therefore, the long-term supplementation of vitamin D and iron is recommended, alongside vitamin B1 and B6 supplementation if deficiency symptoms are detected [52]. Existing evidence does not confirm significant benefits from probiotic supplements in postoperative recovery, and they are not routinely recommended [47].

4. Post-Discharge Nutrition Management

Patients who struggle to meet nutritional and energy requirements orally should work closely with registered dietitians for continued monitoring and adjustments to their nutritional plan [47,48]. Individualized dietary regimens, pancreatic enzyme replacement therapy, and necessary micronutrient supplementation should continue after discharge to ensure optimal long-term outcomes [39-42,48].

In conclusion, nutritional management for pancreatic cancer patients undergoing radical surgery should span the preoperative, perioperative, and post-discharge phases, with a focus on individualized and dynamic approaches [38-42,43-46]. By implementing standardized home-based nutritional management—particularly within the critical first

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12 weeks following discharge—it is possible to effectively reduce malnutrition rates and related complications, thereby improving patient prognosis and alleviating financial burdens [43-46,48-52].

7. Conclusion

This article comprehensively reviews nutritional management for patients undergoing radical surgery for pancreatic cancer, emphasizing continuous support from preoperative to post-discharge stages. It highlights early oral intake and preferential enteral nutrition to expedite gastrointestinal recovery, reduce complications, and shorten hospital stays. Additionally, pancreatic enzyme replacement is advocated for patients with malabsorption and steatorrhea, alongside targeted supplementation of vitamins and minerals—particularly vitamin D, B1, B6, and iron. Notably, individualized nutritional plans in the immediate 12 weeks after discharge are crucial to preventing malnutrition and related complications. The article's strengths lie in its evidence-based recommendations, underpinned by multiple studies and guidelines from organizations like ESPEN and IASMEN. However, limitations include insufficient exploration of patient-specific interventions and a reliance on limited high-quality randomized controlled trials. Consequently, the piece calls for more robust research to refine best practices, especially once patients leave the hospital environment. Its core conclusion is that a patient-centered, holistic approach—encompassing early intake, careful enzyme supplementation, and close monitoring—improves surgical outcomes and quality of life. In the future, large-scale trials, personalized protocols, digital health monitoring, and interdisciplinary collaborations are expected to further optimize nutritional support for pancreatic cancer patients, offering potential cost benefits and enhanced prognoses.

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