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**Ocena korelacji i wartości prognostycznej wskaźników stanu
odżywienia i wybranych parametrów klinicznych oraz
znaczenia dietoterapii u pacjentów z nowotworami trzustki**

Assessment of the correlation and prognostic factors value of nutritional
status indicators with selected clinical parameters and the importance of diet
therapy in patients with pancreatic cancer

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Abstract

Assessment of the correlation and prognostic factors value of nutritional status indicators with selected clinical parameters and the importance of diet therapy in patients with pancreatic cancer

Introduction

Pancreatic cancer has a poor prognosis and a low survival rate. Surgical resection is the only chance for a potential cure. Although with a high postoperative complication rate, high mortality. The 5-year relative survival in patients with PC is 10.8% (depending on the stage of diagnosis) and increases to 18% in pancreatic tumors and 45% in ampullary carcinoma in the case of a resectable tumor after resection. The standard treatment for both pancreatic cancers located at the head of the pancreas and periampullary tumors is pancreatoduodenectomy (PD) and distal or total pancreatectomy for other cancers in the pancreas. Many patients report difficulties eating and gastrointestinal complaints during the perioperative period, which lead to nutritional status impairments.

Currently, preoperative malnutrition, excess body weight loss, low albumin (ALB) and total protein (TP) level, BMI >25 also $<18,5$ kg/m², and muscle wasting are among well-known metabolic risk factors of postoperative complications after pancreatic surgery. More than 41% of PC may present excessive body mass before the surgery. Patients with BMI ≥ 25 kg/m², at an older age, and with increased intraabdominal fat thickness, soft pancreatic gland, small size pancreatic duct, and tumors of the papilla of Vater or neuroendocrine tumors are at high risk of POPF. Some authors confirmed the relationship between BMI and POPF incidence but suggested focusing more attention on the role of abdominal fat distribution. Patients with POPF were more likely to have a higher visceral fat area (VFA) especially measured at the level of the coeliac trunk. To assess muscle mass, adipose tissue, and other body composition parameters, it is recommended to use data from bioelectrical impedance (BIA), computed tomography (CT), magnetic resonance imaging (MRI), or dual-energy X-ray absorptiometry (DXA) measurements. Bioelectrical impedance is a non-invasive, portable, quick, and bedside tool to assess body composition.

Most BIA parameters (phase angle, extracellular water, total body water, fat-free mass) are recognized as helpful in nutritional status assessment in surgical and critically ill patients. Bioelectrical impedance was confirmed as a useful complementary tool to assess nutritional status which correlated with survival in cancer patients, especially in advanced

stages. The comprehensive review demonstrated the important prognostic significance of body composition parameters, particularly phase angle and fat-free mass in oncological patients. Decreased levels of these indicators were associated with shorter OS and the occurrence of malnutrition. Despite this, there is insufficient data on approved markers for predicting postoperative outcomes in pancreatic and periampullary tumors concerning body composition. Malnutrition was recorded in over 85% of patients with PC using PG-SGA. In most studies using NRS 2002, approximately 52–88% of resectable PC patients presented a moderate to severe risk of malnutrition, which is consistent with our observations. In the early stage of pancreatic cancer, almost 50% of patients undergoing pancreaticoduodenectomy presented a loss of body mass. In pancreatic ductal adenocarcinoma PDAC, loss of weight occurs in 88.6% of cases, with a median of 6.8 kg. Based on the current knowledge, the mean BMI value in PC patients is 22.9–29.2 kg/m², and this is dependent on the disease stage. Therefore, even BMI correlates with parameters of nutritional status, and weight loss is an insufficiently sensitive predictor of malnutrition in PC patients, particularly for sarcopenia assessment, but can be used as an auxiliary tool. BMI can provide incomplete data, especially for body composition, fat distribution, and fat-free mass resources.

Aim

The study aimed to assess the correlations and prognostic factors of selected clinical parameters and nutritional status in patients with pancreatic and periampullary tumors. Depending on the publications we have distinguished three specific goals:

Publication 1. The purpose of this study was to assess the relationship between nutritional status, body composition and selected clinical parameters in patients with pancreatic and periampullary cancer, as well as describe the differences between resection and non-resection groups.

Publication 2. The aim of our study was to evaluate the prognostic role of nutritional status, selected clinical parameters and body composition assessed bioelectrical impedance on clinical outcomes and major complications after pancreatic surgery in oncological patients.

Publication 3. This article aimed to review available publications and collect practical guidelines for nutrition during the perioperative period in patients with pancreatic head cancer.

Material and methods

This is a prospective study that enrolled patients with resectable pancreatic or periampullary tumors who underwent surgical treatment in our institution. The study was approved by the local Ethics Committee. Patients with neoadjuvant chemotherapy, after palliative resection, with a history of other cancer treatment or major surgery during the last 5 years, and patients who had contraindications to body composition analysis (pregnancy, the presence of metal elements in the body, a cardiac pacemaker) were excluded. Clinical and nutritional parameters and body composition data were included in the prospective database.

Body composition parameters were developed by the bioelectrical impedance analysis device the MALTRON, BIO-SCAN 920. For nutritional status assessment, we used NRS-2002 and SGA, weight loss during the last 6 months, body mass index - actual BMI, and usual BMI (before the diagnosis). The information on NS was collected between 1-3 days before the surgery. Based on cut-offs from WHO all patients were divided into groups with BMI ≥ 25 kg/m² as overweight/obese and normal/underweight (BMI < 25 kg/m²). Using NRS 2002 we divided patients into groups with no risk of malnutrition (< 3 points) and risk of malnutrition (≥ 3 points). Biochemical markers including serum albumin and total protein level were evaluated. Blood samples were collected on the day before or the day of the surgery. Postoperative complications were graded according to the Clavien-Dindo classification. The grade 1 and 2 Clavien-Dindo complications were classified as mild, whereas the grades 3 through 5 were regarded as severe.

The correlation between pairs of variables was assessed by either Pearson's r test or Spearman's rho. Statistical analyses were performed in IBM SPSS Statistics 27.0. To compare groups by nominal data, Pearson's chi-square test or Fisher's exact test was performed if the expected number was lower than 5. Univariate and multivariate logistic regressions were performed to determine CD > 3 predictors.

Results

Publication 1.

We evaluated 76 patients with pancreatic cancer and periampullary tumors. After histopathological and intraoperative diagnosis, all subjects were divided into resection n = 59 (77.6%) and non-resection n = 17 (22.4%) tumor groups. Malnutrition was recorded in 84.2%

(n = 64) and 78.9% (n = 60) using NRS 2002 and SGA. Severe malnutrition (grade C) was detected in 44.7% (n = 34) of overall cases. We recorded the differences in nutritional status compared with resection and non-resection tumor groups. In the SGA case, all patients in the non-resection group had malnutrition. We recorded no differences in body composition between non-resection and resection tumor patients. The analysis showed a series of correlations between nutritional status parameters and age, status performance, tumor stage, and other clinical parameters. We found a positive correlation of body mass loss% with icw, 50 Hz impedance, CRP, and age, as well as a significant negative correlation with fat_kg, tbw_lt, ecw%, ecw/icw, arm, calf, BMI, Karnofsky score, RBC, HGB, and HCT. Malnutrition (SGA) was correlated with AGE, CRP, tumor size and Ca19-9. Positive correlations were also between NRS 2002 and ICW% and negative with ECW%.

Publication 2.

To assess the preoperative nutritional assessment and body composition we enrolled 56 patients with pancreatic and periampullary tumor. BIA measurements in our patients showed no significant disturbances in body composition when we compared them to the healthy population. Overall, postoperative complications occurred in 71.4% (n=40) of cases and severe (Clavien-Dindo ≥ 3) had 28.6% (n=16) of patients. Pancreatic fistulas occurred in 19.6% and septic complications in 41.1% of cases. One-year mortality after surgery was 26.8% in our patients and was not dependent on nutritional status assessed by NRS 2002. NRS ≥ 3 was associated with an inconsiderable incidence of overall surgical complications and has no influence on the type of postoperative complications but prolonged the length of stay in hospital 13 vs 9 days compared to no risk of malnutrition patients ($p = .021$). We observed that tumor location had no significant influence on the risk of malnutrition ($p = .097$). In multivariate analysis the factors predictive of severe complications after pancreatic resection)

Publication 3.

The common symptoms associated with tumors in the pancreas include mechanical jaundice, abdominal pain, loss of appetite, early satiety, unintentional weight loss, steatorrhea, flatulence, changes in taste, hypoglycemia (insulin), and hyperglycemia. Surgical treatment of tumors of the head of the pancreas or ampulla of Vater involves pancreaticoduodenectomy using the Whipple's or Traverso-Longmire method. It has been shown that the pylorus-sparing method results in better weight loss gains than the Whipple method. Pancreaticoduodenectomy may influence the occurrence of eating disorders, causing both short-term and early also late symptoms. The early symptoms include gastroparesis,

pancreatic fistula, biliary fistula, acute inflammation of the pancreatic stump, diabetes mellites, acidosis, peritonitis, and lymphedema. Pancreatic. The dysfunction of exocrine insufficiency may lead to: deficiencies of fat-soluble vitamins, diarrhea, weight loss, and malnutrition.

Conclusion

Patients with pancreatic and peripapillary tumors have a significant risk of malnutrition and weight loss in the perioperative period. There is a relationship between the size also occurrence of metastases and the nutritional status. Age may have an influence on the risk and progression of malnutrition and greater weight loss. Disease progression increases the risk of malnutrition and hypoalbuminemia. A low level of albumin is an independent prognostic factor for serious postoperative complications and mortality. Detecting abnormalities and a detailed nutritional status assessment as well as introducing individual forms of diet therapy, including nutritional treatment, may reduce the risk of postoperative complications, shorten the length of stay in hospital, and improve the quality of life of patients with operable pancreatic cancer.

In the early stage of PC using BIA parameters as the prognostic indicators of postoperative complications seems to be of limited importance. However, monitoring long-term changes in body weight and composition in patients before and after pancreatic surgery due to cancer seems to be justified.

Publication 1.

Patients qualified for pancreatic surgery due to cancer are characterized by abnormal nutritional status and significant weight loss, at the same time relatively high BMI values and normal levels of albumin and total protein. The body composition of patients with pancreatic or ampulla of Vater tumor does not differ significantly between patients with unresectable and operable tumors. Detection of body composition disorders is difficult to identify at an early stage of disease development. Patients with unresectable tumors had a more severe degree of malnutrition, which may be a result of the advancement of the disease. A proper, detailed assessment of the nutritional status of patients qualified for pancreatic surgery, including body composition measurements, is particularly important and should be an indispensable element of individual nutritional therapy at every stage of treatment. Future

studies should include monitoring body composition and changes in the nutritional status of patients with pancreatic cancer scheduled for surgical treatment.

Publication 2.

There are several prognostic factors for operable PC that may be directly or indirectly related to nutritional status. Hypoalbuminemia ($< 3.5\text{g/dL}$) increases the risk of postoperative complications in patients with pancreatic or peripapillary tumors. Patients with malnutrition risk NRS ≥ 3 have significantly lower albumin levels than patients without risk. Therefore, the nutritional status should be assessed and risk factors for malnutrition identified each time before surgery. The role of BIA measurement appears to be limited in patients with early-stage pancreatic tumors or ampulla of Vater, but it may help deepen the assessment of nutritional status and identify extreme body composition abnormalities that may have prognostic value. It should be emphasized that BIA can be a sensitive indicator for monitoring changes in body composition in the postoperative and long-term periods. The presence of diabetes reduces the risk of postoperative complications. Therefore, the identification of glycemic disturbances is an important element of the preoperative assessment of the risk of complications related to surgical treatment.

Publication 3.

Patients after pancreatic surgery may have nutritional deficiencies and ailments that affect their nutritional status and quality of life. Due to the poor prognosis and high mortality among patients undergoing pancreatic surgery due to cancer, it is necessary to use individualized dietary therapy, including clinical nutrition both before and after surgical treatment. Special recommendations and implementing them in practice could improve the nutritional status and clinical parameters and reduce the risk of intraoperative complications. As well as reducing the adverse effects of cancer treatment and improving the quality of life of patients.