Correlation between Pancreatic Cancer and Diabetes - brief review of the last 5 years

Correlação entre Câncer de Pâncreas e Diabetes – breve revisão dos últimos 5 anos

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ABSTRACT
Diabetes mellitus is a group of metabolic diseases defined by persistent hyperglycemia. Severe hyperglycemia leads to classic symptoms such as polyuria, polydipsia, fatigue, and decreased performance. This condition presents, different classifications considering its possible etiologies, being four subtypes: type 1, type 2, gestational and other specific forms of diabetes type 3c. It is suggested that there is a strong association between diabetes mellitus (especially type 2 diabetes mellitus) and carcinogenesis, but this correlation is still underestimated during the diagnosis of diabetes. This paper aims to review the literature on the PubMed search platform for papers from the last five years on the correlation between pancreatic cancer and
diabetes; through the adoption of specific descriptors and rigorous selection criteria of the selected articles to be used as a basis, and thus a total of twenty two articles fit to carry out this work. Based on the current literature, several studies have suggested that diabetes mellitus and cancer are often coexisting diseases, but they are rarely diagnosed concurrently and consequently make treatment difficult and the prognosis tends to be unfavorable, which makes greater disclosure about the correlation essential. Among such diseases, aiming at a better diagnosis in a systematic way, and thus making the patient's prognosis more reliable.

**Keywords:** Diabetes Mellitus, pancreatic neoplasms, glycemia control, hyperglycemia, pâncreas.

**RESUMO**

O diabetes mellitus é um grupo de doenças metabólicas definidas por hiperpílectemia persistente. A hiperpílectemia grave leva a sintomas clássicos como poliúria, polidipsia, fadiga e diminuição do desempenho. Esta condição apresenta diferentes classificações considerando suas possíveis etiologias, sendo quatro subtipos: tipo 1, tipo 2, gestacional e outras formas específicas de diabetes tipo 3c. Sugere-se que exista uma forte associação entre diabetes mellitus (especialmente diabetes mellitus tipo 2) e carcinogênese, mas essa correlação ainda é subestimada durante o diagnóstico de diabetes. Este artigo tem como objetivo revisar a literatura na plataforma de busca PubMed de artigos dos últimos cinco anos sobre a correlação entre câncer de pâncreas e diabetes; através da adoção de descritores específicos e critérios rigorosos de seleção dos artigos selecionados para serem utilizados como base, ficando assim um total de vinte e dois artigos aptos para a realização deste trabalho. Com base na literatura atual, vários estudos sugerem que o diabetes mellitus e o câncer são frequentemente doenças coexistentes, mas raramente são diagnosticados concomitantemente e, consequentemente, dificultam o tratamento e o prognóstico tende a ser desfavorável, o que torna essencial uma maior divulgação sobre a correlação, dentre tais doenças, visando um melhor diagnóstico de forma sistemática, e assim tornando mais confiável o prognóstico do paciente.

**Palavras-chave:** Diabetes Mellitus, neoplasias pancreáticas, controle glicêmico, hiperglicemia, pâncreas.

**1 INTRODUCTION**

It is now known that the diabetes mellitus (DM) epidemic and its complications represent a major threat to global health. The International Diabetes Federation (IDF) estimated that 1 in 11 adults aged 20-79 years (415 million adults) had diabetes mellitus globally in 2015[1,2]. Diabetes mellitus is a group of diseases characterized by sustained hyperglycemia caused by improper function or decreased insulin secretion[2].

Severe hyperglycemia leads to classic symptoms, such as polyuria, polydipsia, fatigue and decreased performance, otherwise unexplained weight loss, visual disturbances and susceptibility to ketoacidosis infections, which can lead to severe coma. The diabetes mellitus is classified into four subtypes: type 1, type 2, gestational and other specific forms of type 3c diabetes [3].
Type 1 diabetes is a disorder of insulin secretion by predominantly immunological mediation through the destruction of pancreatic beta cells with mainly absolute insulin deficiency[1,4,5]. Type 2 diabetes is a decrease in insulin efficacy, insulin resistance, with progressive loss of beta cell function with initially often relative insulin deficiency and a typically glucose-dependent disorder. Gestational diabetes is a glucose tolerance disorder first diagnosed during pregnancy. And diabetes in other specified ways, type 3c, happens due to factors related to syndromes, tumors and tumor pathologies related to the pâncreas [4,5].

Pancreatic cancer remains a highly fatal malignancy and is expected to become the second leading cause of cancer death in the United States in the next twenty to thirty years. The 5-year survival rate at the time of diagnosis is 10% in the USA, since approximately 80-85% of patients have unresectable or metastatic disease[6,7].

And it is known that modifiable risk factors associated with the development of pancreatic cancer may be related to type 2 diabetes, since this disease has been increasingly present in the population's daily routine[8].

2 MATERIALS AND METHODS

This review carried out by the search on the following basis of given it tronica: PubMed and Lilacs, whose descriptors used were: diabetes mellitus, pancreatic cancer, hyperglycemia, glycemic control, pâncreas and metabolismo (Table-1) in order to raise the ratio of tumors of the pancreas and diabetes metabolic disease, addressing definitions, etiology, diagnosis, prognosis and the challenges involved in the correlation between both diseases to date.

Data collection was carried out at different times. First all references were exported to the Mendeley Deskyop 1.13.3 software (Mendeley Ltd., London, England), in order to track possible duplicate records. Subsequently, the titles and abstracts were read in detail to exclude articles outside the scope of the research. In this phase, case report articles were excluded. Studies classified as systematic reviews, original articles and literature reviews that address diabetes mellitus, pancreatic cancer and their correlations were included. There was no language restriction and for the publication period, only articles published in the last five years (2016-2021) were selected. The articles in which the title and the abstract did not present sufficient information had the full text analyzed, in order to decide on its eligibility. Those who presented a title within the theme, but the abstracts were not available, were also obtained and analyzed in full. Articles of interest, present in the references of included studies, and which met the eligibility criteria, were also included in the present study.
3 RESULTS

In total, a total of 22 articles were included in the studies after analysis and application of the inclusion and exclusion methods. Where everyone was related about diabetes mellitus and pancreatic cancer and raised the convergence between both diseases as being of fundamental importance, and that the diagnosis of association between diseases was still uncommon, even though the relationship index is high, thus making a very big challenge in the early approach to cancer treatment and, consequently, control of diabetes mellitus, making the prognosis unfavorable, bearing in mind that each pathology alone presents different levels of judgment, but when they present simultaneously the predictability of a favorable outcome becomes Minimum. An in-depth study of the association between diabetes and risk of pancreatic cancer can become of fundamental importance for two main reasons: the possible use of diabetes of recent onset as a marker of the disease and, in particular, as a specific marker of pancreatic cancer, and the selection of a population at risk for pancreatic cancer.

4 DISCUSSION

Diabetes mellitus is a group of diseases defined by persistent hyperglycemia[9]. The most prevalent form is type 2 diabetes, which is initially characterized by decreased insulin sensitivity and, subsequently, by an inadequate response to compensatory insulin[4,9]. However, diabetes can also develop as a direct consequence of other diseases, including diseases of the exocrine pancreas[10].

The diagnosis of diabetes is based on the analysis of symptoms and tests of fasting blood glucose, oral glucose tolerance test (OGTT) or Hemoglobin A1c (HbA1c)[2-4].

Pancreatic cancer is an intractable malignancy and is the seventh leading cause of cancer deaths in industrialized countries[9]. Although the cause of pancreatic cancer is complex and multifactorial, smoking, to his family and metabolic changes are dominant tory[11,12].

The association between pancreatic adenocarcinoma and diabetes has been recognized for over 150 years. The meta-present in the literature showed a consistently higher risk of 1.5-2 times adenocarcinoma pancreas in diabetes patients with long time (> 5 years) and an increased risk in individuals with diabetes shorter duration to 5 years, or, with a sudden onset, with no previous history within the genealogy[11,13].

However, the association between diabetes and pancreatic cancer remains unclear, due to the bidirectional relationship, since the pancreatic tumor can lead to abnormal glucose metabolism and inadequate glucose metabolism can result in pancreatic cancer. In studies by Zimet [14] and collaborators suggested that the main cause of pancreatic cancer in diabetics is
the high level of insulin and its precursors. In addition, there are authors who present genetic susceptibility to pancreatic cancer in diabetics[8,15].

In other studies, they suggested that insulin resistance and diabetes may be induced by precancerous conditions or undiagnosed pancreatic cancer, although the risk of pancreatic cancer has been shown to be 1.5 to 2 times higher in type II diabetes, even when impaired glucose tolerance is detected more than 5 years or 10 years before the onset of cancer[16,17].

The diagnosis of pancreatic carcinoma is made by ultrasound, computed tomography, cytology, biomarkers [18].

The biomarker as an amyloid polypeptide of the tissue islets decreased in the early stage of pancreatic cancer [18,19]. The increase in the serum glucagon / insulin ratio and the increase in the serum A 14-amino acid peptide of s100A8 identify pancreatic cancer in patients with recent onset DM. The increase in serum adrenomedullin and the increase in Vanin-1 and matrix metalloproteinase 9 are potential biomarkers of DM related to pancreatic cancer. Higher serum levels of CA 19–9 and / or CEA and serum Erc / mesothelin are useful in screening for initial pancreatic carcinoma. New onset of DM is associated with a large tumor and increased CA 19-9[19,20]. Corroborating with several studies, which increasingly relate the onset of diabetes mellitus with a possible diagnosis of pancreatic cancer, the study and applicability of markers for a better and faster diagnosis being of fundamental importance.

Despite 10-25% 5-year survival rates for patients who can undergo surgical resection, surgery remains the only treatment that offers curative potential[20]. The status of resectability must be determined by a multidisciplinary team after evaluation with a high-quality cross-section image[17,18].

Since diabetes improves after pancreatic resection, which suggests that diabetes mellitus is both a consequence and a cause for pancreatic cancer. N egg beginning of hyperglycemia and diabetes mellitus are early signs of pancreatic cancer, therefore, are screening tool for high risk cases of pancreatic cancer to determine the mode of treatment and prognosis[22]. Postoperative mortality from pancreatic cancer is higher in patients with diabetes mellitus[22,23].

The potential curative treatment for pancreatic cancer is surgical resection, but the impact remains minimal on overall survival. Other treatment modalities are chemotherapy and new molecular therapies, such as gene therapy, antiangiogenic agents, immunotherapy and cell signaling inhibitors[24]. With surgical resection and complete removal of the tumor, improvement and cure of diabetes mellitus is seen, associated with pancreatic carcinoma.
5 FINAL CONSIDERATIONS

Pancreatic cancer is a silent disease, which makes its diagnosis in the early stages a great clinical challenge, so that the patient can have a better picture of survival, since it is a very aggressive pathology. As said, as it is a condition that is difficult to diagnose early, it is essential that the physician or team of health professionals can relate diabetes conditions that would usually be unconventional, with a tumoral condition, as both pathologies show a unique association and this Thus, greater dissemination and understanding of the correlation between the diseases, may collaborate with more accurate and earlier diagnoses of pancreas-related neoplasms, in patients who only present classic symptoms of diabetes mellitus.
REFERENCES


