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Pancreatic Cancer and its Relationship to New-onset Type 2 Diabetes Mellitus

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Abstract

The fourth leading cause of cancer deaths in the United States is pancreatic cancer [1,2,6]. Typically affecting older adults between the ages of 60-80, pancreatic cancer carries a high mortality partially due to its late diagnosis [1,2]. There is no uniform screening recommendation provided by any medical organization; however cutaneous or endoscopic ultrasounds may prove useful to screen individuals at high risk for developing pancreatic cancer. Several risk factors for pancreatic cancer are non-modifiable such as hereditary or genetic causes while others are modifiable through lifestyle adjustments such as obesity, alcohol consumption, type 2 diabetes, medication use [2,3]. The goal of our study is to further investigate this relationship in our patients in the Rio Grande Valley.

Introduction:

The fourth leading cause of cancer deaths in the United States is pancreatic cancer [1,2,6]. Typically affecting older adults between the ages of 60-80, pancreatic cancer carries a high mortality partially due to its late diagnosis [1,2]. The most common type of pancreatic cancer is ductal adenocarcinoma, which usually arises in the pancreatic head. Several risk factors have been identified for pancreatic adenocarcinoma while other risk factors are still being investigated [1,2]. The disease is often diagnosed at an advanced stage due to the absence of clinical symptoms in most cases. There is no uniform screening recommendation provided by any medical organization; however cutaneous or endoscopic ultrasounds may prove useful to screen individuals at high risk for developing pancreatic cancer. Traditionally, diagnosis has been made with MRI and biopsy which allows for staging of the tumor. At the time of diagnosis, it is fairly common for metastatic lesions to be present. Surgical resection is only therapeutic which is only possible in less than 15% of patients, and therefore treatment is often only palliative [1,3].

Five-year survival rates range from 15-20% depending on the type of tumor, amount of spread, and resectability of the tumor [2]. The five-year survival rate for patients with unresectable pancreatic cancer with distant metastases is approximately 0% [2]. The combined five-year survival rate for pancreatic cancer of all stages is 9%, but the five-year survival rate for pancreatic cancer that is localized at the time of diagnosis is 37% [4].

Several risk factors for pancreatic cancer are non-modifiable such as hereditary or genetic causes

while others are modifiable through lifestyle adjustments such as obesity, alcohol consumption, type 2 diabetes, medication use [2,3]. Some studies suggest that some of the identified risk factors can also be used as prognostic factors [6]. The development of type 2 diabetes mellitus is of particular interest. Literature reveals differing opinions on whether type 2 diabetes mellitus is a risk factor or a consequence of the development of pancreatic cancer [5,6,7]. The goal of our study is to further investigate this relationship in our patients in the Rio Grande Valley.

Current Progress

In order for more clinically accurate and relevant conclusions to be discerned. It was suggested by a research mentor that my research question should be narrowed and more focused. I have been conducting an extensive literature review to understand what information is currently available regarding diabetes and its pharmacologic treatment as it relates to the development or prognosis of pancreatic adenocarcinoma. I have been in contact with the DHR IRB and have made them aware of proposed changes to my protocol. I will submit an amendment once my literature review is complete and if necessary submit an entire new protocol. I have enlisted the help of the UTRGV SOM librarian to further organize my search. I am also in contact with DHR business intelligence in the case of needing to reorder patient data. My plan is to develop and redefine my topic and then collaborate with my colleagues to extract and analyze the data from the EMR. We hope to prepare an abstract and present at a conference in Spring of 2021.

Materials and Method:

Our retrospective chart review of patients with a diagnosis of type 2 diabetes mellitus and pancreatic ductal adenocarcinoma (PDAC) is comprised from patients evaluated by the gastroenterology inpatient and outpatient, hepatobiliary surgical, transplant, and internal medicine services at Doctors Hospital Renaissance (DHR) in Edinburg, TX from January 2015 to February 2020.

Inclusion Criteria

Patients with diagnosis of type 2 diabetes mellitus and biopsy-confirmed pancreatic ductal adenocarcinoma (PDAC) made from January 2015 to February 2020 with the corresponding ICD 10 codes C25.0 - C25.9 were included. Patients who received imaging modality of transcutaneous, abdominal, or endoscopic ultrasound prior to definitive diagnosis with biopsy

were also included. Patients with

Exclusion Criteria

Patients who receive diagnosis of pancreatic cancer other than PDAC such as pancreatic neuroendocrine tumors (e.g. insulinoma, glucagonoma), acinar cell carcinoma, cystadenocarcinoma, pancreatoblastoma, or other exocrine pancreatic tumors (ICD-10 code CD25.4 - “Malignant neoplasm of endocrine pancreas”) were excluded. Patients with PDAC but who also have concurrent diagnoses of other pancreatic cancers, a history of pancreatic resection prior to diagnosis *or* for indications other than removal of pancreatic neoplasm were excluded.

Patients with diabetes other than type 2 diabetes mellitus.

Patients with a history of splenectomy prior to diagnosis and patients who were less than age < 45 at the time of initial pancreatic adenocarcinoma diagnosis.

Data Collection

The variables to be extracted for this study are still to be determined

Results

Before beginning the data extraction from the patient files, it was imperative to really understand the current body of literature available. Below is a list of some of the most relative papers I found and a brief summary.

Topic	Title of Paper(s)	Relevant Conclusion	Citation
Hyperglycemia and Pancreatic Cancer	1. Glycemic Status, Insulin Resistance, and Risk of Pancreatic Cancer Mortality in Individuals with and Without Diabetes	Glycemic status, insulin resistance, and hyperinsulinemia are associated with increased risk of mortality in patients who develop pancreatic cancer	Kim NH, Chang Y, Lee SR, Ryu S, Kim HJ. Glycemic Status, Insulin Resistance, and Risk of Pancreatic Cancer Mortality in Individuals With and Without Diabetes. <i>Am J Gastroenterol.</i> 2020 Nov;115(11):1840-1848. doi: 10.14309/ajg.0000000000000956. PMID: 33156103.
Risk factors in pancreatic cancer	1. Risk Factors in Pancreatic Adenocarcinoma: the Interrelation with Familial History and Predictive Role on Survival 2. Epidemiology of Pancreatic Cancer: Global Trends, Etiology and Risk Factors 3. Diabetes mellitus as a risk factor for pancreatic cancer. A meta-analysis.	New onset diabetes, smoking, family history and age over 60 years are risk factors for pancreatic cancer	Petrusel L, Bilibou M, Drug V, Leucuta DC, Seicean R, Cainap C, Seicean A. Risk Factors in Pancreatic Adenocarcinoma: the Interrelation with Familial History and Predictive Role on Survival. <i>J Gastrointestin Liver Dis.</i> 2020 Sep 9;29(3):391-398. doi: 10.15403/jgld-2529. PMID: 32919422. Rawla P, Sunkara T, Gaduputi V. Epidemiology of Pancreatic Cancer: Global Trends, Etiology and Risk Factors. <i>World J Oncol.</i> 2019 Feb;10(1):10-27. doi: 10.14740/wjon1166. Epub 2019 Feb 26. PMID: 30834048; PMCID: PMC6396775. Everhart J, Wright D. Diabetes mellitus as a risk factor for pancreatic cancer. A meta-analysis. <i>JAMA.</i> 1995 May 24-31;273(20):1605-9. PMID: 7745774.

The case for pancreatic cancer screening	<ol style="list-style-type: none"> 1. Early detection of pancreatic cancer 2. Slight dilatation of the main pancreatic duct and presence of pancreatic cysts as predictive signs of pancreatic cancer: A prospective study 3. Screening for pancreatic cancer. <i>Annals of Surgery</i>, 257(1), 17-26. 	Prediction models, presence of risk factors, and ultrasound changes individually or in combination are all areas that require more investigation to determine its role in screening for pancreatic cancer	<p>Pereira SP, Oldfield L, Ney A, Hart PA, Keane MG, Pandolfi SJ, Li D, Greenhalf W, Jeon CY, Koay EJ, Almario CV, Halloran C, Lennon AM, Costello E. Early detection of pancreatic cancer. <i>Lancet Gastroenterol Hepatol</i>. 2020 Jul;5(7):698-710. doi: 10.1016/S2468-1253(19)30416-9. Epub 2020 Mar 2. PMID: 32135127; PMCID: PMC7380506.</p> <p>Tanaka, S., Nakao, M., Ioka, T., Takakura, R., Takano, Y., Tsukuma, H., Fukuda, J. (2010). Slight dilatation of the main pancreatic duct and presence of pancreatic cysts as predictive signs of pancreatic cancer: A prospective study. <i>Radiology</i>, 254(3), 965-972. doi:10.1148/radiol.09090992</p> <p>Poruk, K. E., Firpo, M. A., Adler, D. G., & Mulvihill, S. J. (2013). Screening for pancreatic cancer. <i>Annals of Surgery</i>, 257(1), 17-26. doi:10.1097/sla.0b013e31825ffbfb</p>
Pancreatic Cancer and Diabetes	Pancreatic Cancer and Diabetes	Diabetes mellitus type 2 is postulated be a risk factor, prognostic factor and sequelae of pancreatic cancer.	Sharma A, Chari ST. Pancreatic Cancer and Diabetes Mellitus. <i>Curr Treat Options Gastroenterol</i> . 2018 Dec;16(4):466-478. doi: 10.1007/s11938-018-0197-8. PMID: 30215162; PMCID: PMC6436833.

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De Souza, A., Irfan, K., Masud, F., & Saif, M. W. (2016). Diabetes Type 2 and Pancreatic Cancer: A History Unfolding. *JOP : Journal of the pancreas*, 17(2), 144–148.
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Discussion

Pancreatic cancer is one of the leading causes of cancer death in the United States.

Unfortunately, by the time most cases are diagnosed patients typically have very advanced disease thus leading to its poor prognosis [2,4]. Today there is no widely accepted screening criterion for pancreatic cancer thus most cases come to clinical attention due to the structural or functional impairment of affected tissue. Although type 2 diabetes mellitus relationship to pancreatic cancer is well documented in the literature, its exact pathophysiological relation to the disease is still a topic of debate. Further outlining correlations and prognostic indications of the aforementioned disease states to one another can aid in the future development of screening criterion. Late detection of pancreatic cancer has a very bleak prognosis. Uncovering evidence based screening modalities for this deadly malignancy can save thousands of lives worldwide annually.

References

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