ASSOCIATION BETWEEN PANCREATIC CANCER AND DEPRESSION

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ABSTRACT

Background: Pancreatic cancer has very poor prognosis. Also, the surgical intervention is very high as compared to other cancers. This is associated with high depression and anxiety in the patients. In this study, we tried to study the effects of depression in benign and pancreatic cancer patients. **Methods:** We took a total of 56 patients who were diagnosed to have pancreatic cancer. PHQ-9 score was measured in all the patients at the time of the diagnosis. We even measured the PHQ-9 scores of the patients 3 months and 6 months post-operatively. Responses were analysed by two-way ANOVA and Spearman Correlation coefficient. **Results:** Out of 56 patients, 37 patients were diagnosed to have pancreatic cancer and 19 patients were diagnosed to have benign pancreatic lesion. The PHQ-9 scores in Benign Pancreatic lesion and Pancreatic Carcinoma patients were 18±1.47 and 19±2.12 respectively. Post-operatively after 3 months, the scores were 18±1.68 in Benign Pancreatic lesion and 22±1.24 in Pancreatic Carcinoma patients. At 6 months post-op, the scores were 16±1.26 in Benign Pancreatic lesion and 25±1.47 in Pancreatic Carcinoma patients. The p-value was calculated and it was 0.023. **Conclusion:** There is a high incidence of depression in the pancreatic cancer patients since diagnosis and it increases after 3 months and 6 months post-operatively as compared to benign pancreatic lesions.

KEYWORDS: Pancreatic cancer, anxiety, pancreatic.

INTRODUCTION

Although pancreatic carcinoma and depression have been linked for many years, the prevalence and relationship of these two entities are still poorly understood. Published studies reviewing this issue have found that many patients with pancreatic cancer are depressed. A clinical gestalt asserts that many patients present with depression before pancreatic carcinoma is diagnosed. If the definition of depression is broadened to include mild depression in addition to major depression, these numbers may increase. Depression in pancreatic cancer is a condition that must be diagnosed and treated, as studies have shown that depression is a detrimental factor in the last stages of life of cancer patients as patients with high score of depression have worse survival rates in breast and hepatobiliary cancers. Treatment for depression has also been shown to impact quality of life and may bring increased comfort during end of life. This article reviews the literature linking pancreatic carcinoma to depression as well as the appropriate therapeutic approach. In addition, for the first time, it fully underlines the key role of a social worker as a key participant throughout the cancer continuum: at time of diagnosis, treatment, relapse, survivorship, end of life and bereavement in the management of pancreatic cancer patients.

Several studies, dating back as early as the 1930s, have been conducted in order to examine the association between depression and pancreatic cancer.[1] A study in 1967 showed that more than half of patients with pancreatic cancer had psychological symptoms occurring as early as 43 months before physical symptoms.[2] When depression is considered a normal phenomenon in cancer patients, its impact on the quality of life is trivialized. This review studies the literature regarding the association between depression and pancreatic cancer as well the appropriate therapeutic approach.

Incidence Depression has long been known to have greater incidence in pancreatic cancer patients than in patients with other malignancies. Frase conducted a

study based on patients admitted for possible pancreatic or colon cancer and found that 76% of patients with pancreatic cancer had depressive symptoms prior to surgery as compared to 20% of colon cancer patients. A retrospective study comparing patients diagnosed with pancreatic and gastric cancers reached the conclusion that depression was initially present in 14% of patients with pancreatic cancer but in only 4% of stomach cancer patients. In 1986, two prospective studies concerning the incidence of depression in gastrointestinal tract malignancies were conducted. Joffe et al. concluded that 50% of patients who were finally diagnosed with pancreatic cancer met the criteria for the diagnosis of depression while none of the patients that were finally diagnosed with gastric cancer met the criteria.[3,4] Holland et al. found that patients with pancreatic cancer in advanced stages have more severe depression, anxiety and total mood disturbance as compared to patients with other advanced abdominal neoplasms. In 1993, 52 pancreatic cancer patients were studied, out of which 71% had depressive symptoms and 48% had "anxiety-related" symptoms.[5] According to Massie , the prevalence of depression in people with pancreatic cancer ranges from 33% to 50%. Paraneoplastic Syndrome Depression.[6] Depression may be a manifestation of a more generalized paraneoplastic syndrome, which consists of remote effects of the tumor without direct metastatic activity. Depressive symptoms are found in 58% of paraneoplastic limbic encephalitis cases. Paraneoplastic limbic encephalitis is also characterized by anxiety, irritability, hallucinations, memory loss, seizures, episodes of depersonalization and, sometimes, dementia. It is most common in lung, breast and testis cancer. Paraneoplastic limbic encephalitis's symptoms usually precede the diagnosis of cancer while the tumor might still be undetectable. Thorough testing must be performed until the malignancy is diagnosed. Diagnosis of paraneoplastic limbic encephalitis requires neuropathological exams or the presence of the four following criteria: 1. compatible clinical presentation; 2. interval of less than 4 years between the development of neurological symptoms and cancer diagnosis; 3. exclusion of other neuro-oncological problems. at least one of the following: cerebrospinal fluid with inflammatory changes but no positive cytology, MRI with temporal lobe abnormalities or EEG with epileptic activity in the temporal lobe . Pathophysiology is believed to be immunological with cancer-induced auto-antibodies attacking the patient's central nervous system.

Diagnosis of Depression in Cancer Patients has been found to worsen a patient's pain and should not be considered "normal" in the terminally-ill. After the diagnosis of cancer, there is usually a process that patients go through in order to cope: initial shock and denial of diagnosis, anxiety and depressive symptoms, impaired cognitive ability, a decreased appetite and a disrupted sleep pattern. In 50% of patients, these symptoms subside within 10 days with family support and treatment that offers hope. The actual level of psychological distress experienced by the patient depends on: 1. medical factors: advanced disease, treatment, pain, physical disability, family history of depression; 2. psychological factors: such as a patient's coping ability or history of depression. The patient's perception of cancer and its manifestations is significant, mainly fear of losing control over body functions and of painful death; 3. social factors: whether emotional and financial support from family and friends is available . The physician should be able to recognize when this distress exceeds "normal". Intervention is needed when depressive symptoms are highly disruptive or when their intensity and duration are greater than expected, provided that these do not qualify for diagnosis of a depressive episode (Diagnostic and Statistical Manual IV). Major depressive disorder is 4 times more often in cancer patients. While diagnosis of depression in physically healthy patients is based on symptoms like anorexia, weight loss and fatigue, which are common in cancer, psychological or cognitive symptoms of depression (hopelessness, loss of self-esteem, anhedonia, guilt, suicide ideation) are the basis for diagnosing depression in cancer patients. A physician should not be afraid to ask a patient about suicidal ideation out of fear of "giving him the idea", because, on the contrary, this gives him the chance to talk about his feelings and these thoughts are justified. Some sub-threshold forms of depression, which go undiagnosed and untreated, are often observed in cancer patients. These can be prodromes of major depression, residual symptoms post treatment or a new medical condition altogether

METHODS

In this study, we took a total of 56 patients who were diagnosed to have pancreatic lesions. 37 patients had pancreatic cancer and 19 patients had benign pancreatic lesions. For diagnosis, CA 19-9, CT-scan of abdomen and CT-guided biopsy was done. For metastasis diagnosis, screening CT scan was done. At the time of declaration of diagnosis, PHQ-9 scores of the patients were measured. PHQ-9 were measured again 3 months and 6 months after operation. Responses were analysed by two way ANOVA and Spearman Corelation coefficient.

RESULTS
Baseline characteristics of all the candidates are shown in the table below.

Table 1: Baseline characteristics of the patients.

Variable Name	Males (N=29)	Females (N=27)
Age (yrs)	56±5.97	58±6.87
Active Smoker	15(51.72%)	17(62.96%)
History of Alcohol Consumption	8(27.58%)	2(7.40%)
History of Gallstone disease	3(10.34%)	14(51.81%)
Family History of Pancreatic Cancer	2(6.89%)	1(3.70%)
BMI	26±5.68	28±4.59

As per table 1, there were 29 males and 27 females in our study. The average age in males was 56±5.97 years and in females was 58±6.87 years. There were 15(51.72%) active smokers in males and 17(62.96%) in females. 8(27.58%) males had a history of alcohol consumption. 2(7.40%) females had a history of alcohol consumption. 3(10.34%) males had a history of gallstone disease and 14(51.81%) females had a history of gallstone disease. 2(6.89%) males had a history of pancreatic cancer in family and 1(3.70%) females had a history of pancreatic cancer in family. Average BMI was 26±5.68 in males and 28±4.59 in females.

The results of all the PHQ-9 scores at various time periods are depicted in the table below.

Table 2: PHQ-9 score co-relation.

	PHQ-9 score at time of diagnosis	PHQ-9 score at 3 months post-operatively	PHQ-9 score at 6 months post-operatively	P value
Benign Pancreatic lesion (N=19)	18±1.47	18±1.68	16±1.26	0.023
Pancreatic Carcinoma(N=37)	19±2.12	22±1.24	25±1.47	

PHQ-9 scores at the time of diagnosis were **18±1.47** in patients with benign pancreatic lesions and **19±2.12** in patients with pancreatic carcinoma. At the end of 3 months after operation, it was **18±1.68** in patients with benign pancreatic lesions and **22±1.24** in patients of pancreatic carcinoma. At the end of 6 months after operation, it was **16±1.26** in patients with benign pancreatic lesions and **25±1.47** in patients with pancreatic carcinoma. The p value 0.023 (<0.05) which is highly significant. This shows that the difference in the scores between the groups was real and not due to chance.

DISCUSSION
It can be inferred that in the beginning when the diagnosis was uncertain as whether it was a benign lesion or a malignant lesion, the PHQ-9 scores were almost same in both the age groups. But 3 months after surgery, the scores were lower in benign pancreatic lesion patients as compared to the patients with pancreatic cancer. This was more evident at the end of the 6 month period. When the PHQ-9 scores increased in the pancreatic carcinoma group and decreased in the benign pancreatic lesion group. This shows the anxiety and stress related to the bad prognosis of the pancreatic carcinoma.

Pancreatic cancer patients had significantly higher levels of IL-6 and IL-10 and significantly lower TGF-beta levels than healthy participants. When the sample was divided into those with and without MDE, the groups only differed with regard to serum IL-6 levels. No significant cancer and depression interaction effect was observed. Severity of depressive symptoms was also significantly correlated with IL-6, $r_s = 0.28$ and $p = 0.02$, whereas hopelessness was associated with IFN-alpha, $r_s = 0.34$ and $p = 0.006$. Pain, fatigue, and sleep disturbance were associated with several of the cytokines assayed including IL-1beta (pain intensity), IL-4 (pain intensity and overall sleep quality), IL-12p70 (pain intensity), and TGF-beta (fatigue intensity), but anxiety was not associated with any of the cytokines assayed. Cancer patients with depression had markedly higher plasma concentrations of IL-6 than healthy comparison subjects and cancer patients without depression. Although significant correlations were found between Hamilton depression scale scores and plasma concentrations of postdexamethasone cortisol, no significant correlations were found between plasma IL-6 and postdexamethasone cortisol. Men with mental disorders were more likely to develop pancreatic cancer than those without psychiatric claims (odds ratio 2.4, confidence interval 1.15–4.78). Depression more commonly preceded pancreatic cancer than it did other gastrointestinal malignancies (odds ratio 4.6, confidence interval 1.07–19.4) or all other cancers (odds ratio 4.1, confidence interval 1.05–16.0).

CONCLUSIONS
There is a high incidence of depression in the pancreatic cancer patients since diagnosis and it increases after 3

months and 6 months post-operatively as compared to benign pancreatic lesions.

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