

Review Article

Open Access, Volume 2

Psychological adverse effects of anxiety and stress in treating patients with cancer

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Received: Feb 03, 2022

Accepted: Mar 04, 2022

Published: Mar 11, 2022

Archived: www.jclinmedimages.org

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Abstract

Psychological factors such as chronic stress, anxiety and depression are major risks that could lead to cancer if not promptly treated. These risks could also cause cancer to become more aggressive and hence more resistant to anti-tumor therapy. For these reasons, it's highly recommended that cancer patients should either have thorough psychological assessment before commencement of their cancer treatment, or, if cancer treatment couldn't be postponed, be assessed contemporaneously to allay any risk factors which could result in unfavorable treatment mishaps. In some cases, though, psychological treatment could take some time before cancer treatment commences, to ensure that patients are totally prepared to deal with cancer treatment under favorable psychological conditions. According to current cancer practices, one or more psychological and/or psychiatric department(s) for diagnosing and treating cancer patients should be within close distance from the cancer centers. Such an approach have proven to be effective in having quintessential anti-tumor cancer treatment results emanating from the improvement of cancer patients' mental health. Studies have also shown that cancer patients, who go through psychological assessment, end up having better quality of life and extended life expectancy. The use of telemedicine to carry out online counseling for stress, anxiety and depression in cases where physical access to patients is either difficult or constrained, has also been an excellent conduit for diagnosing and treating cancer patients that go through severe psychological stress and anxiety.

Keywords: psychological therapy; anxiety; stress; cancer; cortisol.

Introduction

Contemporary research on stress that dates back 30 years, have shown irrefutable evidence that psychological factors influence the development and/or progression of cancer [1]. Many scientists and researchers alluded to chronic daily life stresses such as, death of a loved one, a job loss, divorce, excessive unmet financial obligations, chronic illnesses or injuries,

moving to a new home, getting married, are factors that certainly lead to anxiety, depression, anger, low self-esteem, guilt, grief, as well as social isolation, which would have grave and expedited cancer progression or even lead to early metastasis. On the other hand, patients with cancer end up having negative psychological state that tends to cause emotional problems, notably: anxiety and stress. The initiation, as well as taking the decision to continue anti-tumor therapy, can literally cause undue

anxiety too. The recent pandemic that led to COVID-19, have also exacerbated further emotional stress even in all patients, including oncological ones.

Accordingly, theoretical and empirical studies could certainly help support stress-management intervention as well as provide assistance to clinical cancer care in the future to come [2].

Material and methods

This article exhibits the relationship between psychological stress and the risk of development and ensuing progression to cancer. To ascertain this, we have carried out our own analyses by using the internet and PubMed database relating to the latest evidence revealed in various publications pertaining to year periods of 2007 to 2021. To do that, we have used the following key words: psychological therapy, anxiety, stress, cancer, cortisol to cover the extensive review of nineteen articles based on inclusion/exclusion criteria.

Results

Epidemiological observations relating to the effects of behavioral and psychosocial changes on cancer development, progression, and death rates continue to evolve [1]. According to Kruk J. et al., these factors reflect the risks associated with specific types of cancers [1]. Kruk also states that any change in social and psychological behaviour, should be considered in the realm of psychological stressors. These factors interact with molecular mechanisms which are very important factors that help in understanding cancer management and hence cancer prevention [1].

Interaction between chronic stress on carcinogenesis and psychosocial factors have also been probed with some interesting results that implicate the function of the hypothalamic-pituitary-adrenal axis, the sympathetic axis and natural killer cells [1]. Stressful psychological situations generate upregulation that lead to the release of catecholamines, such as, adrenaline, noradrenaline, which are proven to activate the body's hypothalamic-pituitary-adrenal axis, as well as the production of reactive oxygen species and the dysregulation of the sympathetic system, that disturb cell homeostasis causing pro-inflammatory proteins produced by the cells, thus reducing immunity protection [1]. The main immunological mechanism, which is not functioning properly in chronic psychological stress, is cellular immunity [1]. A new study have identified a glucocorticoid-inducible transcriptional regulator called TSC22D3, which is activated by stress, that affects dendritic cells that create body immunosuppressive condition that prohibits the organism from detecting and destroying cancer cells [3].

Chronic stress may also stimulate incessant growth of circulating proinflammatory factors, such as, IL-1 β , IL-6, and C-reactive protein, that shift the cytokine balance from Th1 cytokines, which promote tumor-protective cell mediated immunity, to Th2 cytokines, which promote antibody mediated immunity [2]. Short-term elevations in IL-6 and IL-1 β are hence essential for initiating and maintaining immunoprotective mechanisms. On the contrary, however, these factors' chronic rise could cause chronic inflammation, which are known to be responsible for proinflammatory and autoimmune disorders that reduce posi-

tive cancer outcome in patients with reported malignancies [2].

The pattern of success of any cancer therapy includes, amongst other things, a package of immunoprotective responses (for instance immunotherapy), which aim at rendering cancer cells immunogenic and hence susceptible to auto-removal by the immune cells [2]. Thus, chronic stress which suppresses the protective effect of the immune cells continues to remain a critical pathway for exacerbating tumor development, progression, and metastasis [2]. Recent studies have analysed the critical role of psychological stressors in association with protective immunity in squamous cell carcinoma (SCC), basal cell carcinoma (BCC), as well as tumours associated with human papillomavirus (HPV) [2]. Other indices of inflammation such as neutrophil-to-lymphocyte ratio and albumin could help health professionals manage successfully oncological patients that have anxiety and depression disorders at Cancer Centres with close visits to psychiatry [4]. It has been shown that a hypoalbuminemia state seen in patients with metastasis is closely correlated with incessant persistence of depression, anxiety and psychiatric treatment management [4].

Recent studies in patients with ovarian cancer with shorter survival and life expectancy, for instance, were correlated with diurnal cortisol profiles and interleukin-6 plasma levels demonstrating that women with chronic anxiety during the first year after diagnosis exhibited greater risks for negative cancer treatment outcomes [5]. Similar studies using animal models or cancer cell lines also provided correlation in stress processes, molecular mechanisms and immune measures in oncology [2]. Therefore, it is necessary having early psychological assessment, in patients with cancer metastasis, in order to obviate any disorders that could interfere and have a negative impact on patients' cancer progression and prognosis [6].

Yang et al. has exhibited quantitative epidemiological study based on observations emanating from job stresses and their association to cancer [7]. The author found significant statistical effects of job stresses that translate into higher risks to multiple types of tumours; inter alia: colorectal cancer, RR = 1:36 (1.16-1.59); lung cancer, RR = 1:24 (1.02-1.49); esophageal cancer, RR = 2:12 (1.30-3.47). Other types of cancer such as prostate, breast, or ovarian cancers were found not to be influenced by workers' mental health [1].

Further updates have also shown that people, who experience stress, encounter shorter nucleotide sequences (telomeres) by looking 10 year older as compared to those with low stresses [8,9]. Collective action of telomeres degradation, oxidative stress, elevated levels of proinflammatory cytokines, dysregulation of stress hormones not only lead to quicker aging, but also to oncogenesis [10]. This accumulation of cellular damage is the process that transforms normal cells into cancerous ones [10,11].

Comorbidity of cancer with psychological factors may also interfere with oncological treatment. There is strong evidence that oncological patients, who delay their treatment, or get poor appraisal, encounter difficulty in coping with cancer [12]. In particular, chemotherapy compared to other treatments have shown higher anxiety levels [13]. Studies have also shown

that mental health diagnosis and treatment were prevalent in all types of oncological patients with genitourinary, breast, ovarian and haematological malignancies [5,14,15]. Several psychosocial factors, notably psychosocial support imparted to cancer patients, influence their decision making on the move from surveillance to active treatment [14].

A Chinese research article showed that amongst 6,213 cancer patients, 23.4% had depression, 17.7% had anxiety, 9.3% had post-traumatic stress disorders, and 13.5% exhibited aggressive attitudes [15]. There are several types of treatments and approaches imparted to cancer patients that could cause escalation in psychiatric disorders. For instance, Klaassen Z et al., showed that 19% of patients undergoing radical cystectomy were more likely to present psychiatric disorder as compared to those choosing alternative methods, such as a combination of radiotherapy and chemotherapy [15]. Similar evidence in other studies had shown that anxiety had negative effects on breast cancer treatment approaches [13]. Each treatment modality, such as, surgery, chemotherapy, radiotherapy or a combination of any of these contributed to various types of anxiety [13]. Several articles analysing this phenomenon revealed that women with breast cancer who chose to go for such breast cancer treatments before the operation had exhibited higher anxiety as compared to those who chose mastectomy [13].

During the covid-19 pandemic, oncological patients showed despondency as well as pre-existing emotional problems associated with the treatment and the progression of cancer [6], [15]. Health measures during the pandemic, such as, physical distancing, decreased motivation, increased mental health distress contributed to loss of self-esteem [15]. Tele-consultations for cancer patients with psychological stress during covid-19 pandemic, reported a mixture of positive as well as negative experiences [16]. On the negative side, patients experienced less confidence and heightened anxiety during such consultations [16]. Caregivers tending to cancer patients have exhibited health problems that adversely affected their patients' health [17]. Families coping with one or more of their members having cancer, reported experiencing communication issues as well as rigidity during the pandemic [18].

Psychiatric illnesses, such as depression and anxiety, are common, but often neglected. Complications emanating from cancer influenced quality of life, the adherence to treatment, cancer survival, and the treatment costs [19]. Depression and anxiety independently from palliative or curative treatment, affect up to 20% and 10% cancer patients respectively [19]. Depression or anxiety also increases suicide risks in specific demographic populations [19].

Discussion

In Pandemic times, cancer patients' emotional state has reported severe deterioration. Rates of anxiety and depression incidents were very high in patients with metastatic cancer who started anti-neoplastic treatment.

This review article demonstrates the relationship between psychological stress and the risk of development and progression to cancer.

The articles we analysed strongly concur with the conclusion that negative psychological factors play an important role in the ineffectiveness of anti-tumor treatments. Factors such as

anxiety, stress and depression can have negative effects on the strength of the immune system, with negative results during the treatment process. Eventually, this causes expedited tumor growth and rapid progression to metastasis.

Stressful situations trigger production of catecholamines: adrenaline and noradrenaline. Further more, the oxidative stress interact with immune system's response thus operating at the cellular level creating an alteration of the body's homeostasis. Studies have shown that chronic and incessant stressful situations adversely affect the regulation of the immune system. We have already revealed how dendritic cells normally act by attacking cancer cells in cancer patients. Stressful situations deactivate the effectiveness of this process to the detriment of the patient. In such cases, tumor growth could no longer be controlled and could escape the immune system's body surveillance mechanism.

If we apply adequate psychological therapies to manage these psychiatric pathologies, we could have auspicious impact on cancer patients. This is why, it has been shown that by using appropriate psychological treatments after diagnosing anxiety, stress or depression, we could achieve optimal treatment anti-tumor result.

From our professional experience standpoint, patients diagnosed with advanced cancer, quite often suffer from anxiety, stress or depression. If it is not the stress, the anxiety or depression, in these advanced stages of cancer, it is the low quality of life, the decrease in anti-tumor therapeutic compliance and the healthcare cost which could lead to ultimate failure. In addition to that, there has been a surge in suicide risks in patients experiencing depression and cancer.

Online consultations for the diagnosis and treatment of these pathologies are considered excellent ways that started during the pandemic for COVID-19. Thus allowing the management of psychiatric pathologies that can have negative effects on the safe anti-tumor treatment.

We are convinced that in oncological practices there should be at least one psychological / psychiatric department for the diagnosis and treatment of these pathologies.

Several past depression and anxiety predictors in oncological patients have been presented in various articles. Few studies have revealed that markers such as age, gender, educational level, are associated with the psychological status and influence of these patients. Positive psychological conditions, such as hope, high self esteem, optimism, and social support, have shown to temper anxiety and depression levels in cancer patients. Hence, psychosocial assessment of cancer patients and the ensuing interventions such as support groups and counselling is paramount in the treatment process of cancer patients.

We hope that in the future other additional studies will shed more light on the different types and range of stress that could affect cancer development and treatment outcome in cancer patients. This would also identify more culprits that could stifle treatment of cancer patients.

Conclusions

This review article presents the relationship between chronic daily life stresses, severe life events, depression, and social isolation as well as the risks of development and progression to

cancer. Results from recently published observational epidemiologic studies, has been the theme of this review. In this article we also analyzed the need procured for the effective management of cancer patients. It has been clearly revealed that negative psychosocial factors, such as stress, anxiety and depression adversely affect the main activity of the immune system that controls the response to anti-neoplastic treatment. Future interdisciplinary research will help scientists further understand how to improve the quality of life of oncological patients by promoting the benefits of psychosocial intervention. Political measures during Covid-19 pandemic should take in account the serious ramifications of isolation that also lead to anxiety and depression in cancer patients, by devising mechanisms that allay risks associated with such conditions.

In conclusion, we believe that further future researches and reviews would be essential so that new intervention ways could be devised to help alleviate stress and anxiety among cancer patients.

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