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Radiotherapy induced fatigue and its correlates

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ABSTRACT

Up to 80% and 30% of patients, respectively, reported experiencing radiotherapy-induced weariness during radiation therapy and at follow-up visits, which is a frequent early and chronic side-effect of irradiation. Medical and nursing personnel commonly underestimate it; just around 50% of patients discuss it with a doctor, and barely one-fourth of those cases result in the patient being recommended any intervention. Rarely do patients anticipate feeling tired as a side effect of treatment. Weak understanding exists on the genesis, correlates, and prevalence of this frequent symptom. Numerous studies have shown that the location of the tumor and the type of treatment used affect the degree and timing of fatigue. In contrast, individuals receiving radiotherapy for prostate cancer may experience exhaustion due to a reduction in neuromuscular efficiency rather than psychological factors. For instance, psychological mechanisms have been hypothesized to explain fatigue in women receiving radiation therapy for early breast cancer. More than pain, erectile dysfunction, and other cancer- or treatment-related symptoms, exhaustion can have an overall negative impact on quality of life. Recently published randomized studies on the management of radiotherapy-related fatigue have explored a number of strategies. Although the best approach has not yet been identified, relaxation treatment, group psychotherapy, physical activity, and sleep have all shown some encouraging outcomes. It is necessary to conduct additional methodologically sound research to better understand the causes, ideal prevention, and management of this symptom.

Key words: breast cancer, radiation therapy, fatigue, anxiety, depression sleep quality, nutritional status

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INTRODUCTION

Cancer of the Breast is the second most frequent type of cancer among women globally and the primary cause of cancer death in these individuals. Breast cancer is the second most common cause of death from cancer in women, exceeded only by lung cancer, with approximately 316,000 patients diagnosed with breast cancer annually [1]. Treatment for breast cancer is dependent on the stage. Stage 0 includes Ductal carcinoma in situ, (a non-invasive malignancy that can advance to invasive cancer in up to 40% of patients) is treated with lumpectomy and radiation or with mastectomy. Ductal carcinoma in situ when Estrogen receptor–positive (ER positive), patients can also receive endocrine therapy. Early invasive stages (I, IIa, IIb) and locally advanced stages (IIIa, IIIb, IIIc) are non-metastatic which have three treatment phases (preoperative, surgical and postoperative phase). The preoperative phase utilizes systemic endocrine or immunotherapies when tumours express estrogen, progesterone, or ERBB2 receptors. Preoperative chemotherapy may also be used and is the only option when tumors have none of those three receptors. The surgical phase has two options with similar survival rates; a lumpectomy with radiation if the tumor can be excised completely with good cosmetic results, or a mastectomy. Radiation, endocrine therapy, immunotherapy, and chemotherapy are part of the third phase i.e. postoperative phase. Stage IV (metastatic) breast cancer is treatable but not curable. Treatment goals include improving the length and quality of life [2].

LITERATURE REVIEW

Breast cancer is a leading health concern among women due to its high mortality and morbidity rate. The five-year survival rate in metastatic breast cancer is less than 30%, even with adjuvant chemotherapy [3]. Breast cancer incidence is more common in high-income countries [4] than in low-income counties, Epidemiological studies correlated different factors for breast cancer risk development or progression [5, 6]. Risk factors including late age for marriage, first childbirth, and menopause are strongly associated with disease development [7-9] (Figure 1).

Radiotherapy related fatigue

Fatigue, characterised by tiredness, weakness or lack of energy, involves physical, cognitive and emotional aspects. Its aetiology is not well defined and the prevalence ranges from 30%–70% in women with breast cancer, reaching up to 80% when they are undergoing radiotherapy. This is one of the most frequent side effects of radiotherapy, and it may interfere with self-esteem, social activities and quality of life [10]. Adjuvant Radio-Therapy

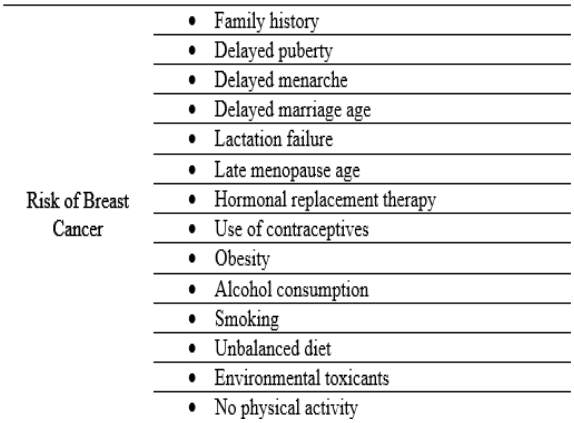

Fig. 1. Schematic representation of breast cancer risk factors

(RT) is the standard treatment for more than 90% of Breast Cancer (BC) patients, aiming to decrease locoregional recurrence and improve overall survival [11, 12]. Despite its beneficial role, numerous side effects are associated with RT, and among the most common is Right-Induced Fatigue (RIF) [13]. In particular, up to 77% of BC patients who undergo RT suffer from RIF as a disorder, characterized by a state of generalized weakness with a pronounced inability to summon sufficient energy to accomplish daily activities [11, 14]. Despite the high incidence rate, the symptom lacks a clear definition. The National Comprehensive Cancer Network (NCCN) defined RIF as a clinical subtype of Cancer-Related Fatigue (CRF) that either arises during RT (acute RIF) or continues afterwards (chronic RIF). RIF is a distressing, persistent, and subjective sense of physical, emotional, or cognitive tiredness or exhaustion, related to cancer or cancer treatment that is not proportional to recent activity, and interferes with normal functioning [15, 16]. Although RIF possibly compromises patients' treatment adherence, it is still underreported, underdiagnosed and undertreated [10, 17].

Radiotherapy induced fatigue-pathophysiology: Multiple factors have been proposed to cause RIF. Some factors include genetics (e.g., DNA damage and telomere length), hypothalamic-pituitary-adrenal axis dysregulation, 5-hydroxytryptophan neurotransmitter dysregulation, and alterations in the Adenosine Tri-Phosphate (ATP) muscle metabolism. Other factors include endocrine disturbances (reduction in estrogen and testosterone), mitochondrial dysfunction, cytokine dysregulation, inflammation and immune response, anaemia, circadian rhythm disruption, disruption in the blood-brain barrier, and psychological mechanisms [13, 18-24].

Radiotherapy induced fatigue severity and assessment: In general, fatigue can be classified according to its severity by using grades from 1 to 3. Grade 1 would be "fatigue relieved by rest," "fatigue not relieved by rest, limiting instrumental activities of daily living" is grade 2, and "fatigue not relieved by rest, limiting self-care activities of daily living" is grade 3. Apart from this classification, objective measurement of fatigue remains a challenge. There is no fatigue-specific standardized assessment tool or scoring system to define the severity grade accurately [19, 25]. For both Cancer Related Fatigue (CRF) and Radiotherapy Induced Fatigue (RIF), assessment by a single-item symptom checklist has led to a certain underestimation in several studies. Currently, subjective questionnaires like the Cancer Fatigue Scale, Multidimensional Fatigue Inventory, Revised Piper Fatigue Scale, Brief Fatigue Inventory, Lee Fatigue Scale, Functional Assessment of Chronic Illness Therapy, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, or the Visual Analogue Scale are used to assess CRF [26-28].

Radiotherapy induced fatigue-impact on patients: It is well known that the prevalence, duration, and severity of fatigue depend on the type of RT, the irradiated volume and dose scheme, and on the combination with other treatments, as patients receiving combined therapies (e.g., chemotherapy plus RT) showed the highest fatigue scores. Pre-treatment fatigue levels have been proposed as an essential risk factor for fatigue development during RT. Diagnosing fatigue and recognizing it as a predictor for this condition during treatment within the first appointments seems to be of uttermost importance. Other factors influencing the grade of severity of RIF that have been described in the literature include the diurnal rhythm, where morning fatigue appears to be more affected by biologic factors and evening fatigue by behavioral factors. Another factor is smoking, with smokers experiencing considerably more fatigue than non-smokers. Time- to-hospitalization appears to influence the grade of severity of RIF, with significantly worse symptoms of fatigue in patients who had to travel 2 hours or more hours compared to patients who had to travel <2 h. Factors such as stress, anxiety, depression, a weakened physical condition, diarrhea, malnourishment, and anemia possibly further deteriorate fatigue [29-32].

Definitive radiotherapy with or without chemotherapy has been found to increase fatigue which further impacted the QOL [33, 34]. Up to 40% of patients were still suffering from RIF 1 year after completing adjuvant RT [35], or even 5 years -10 years following the completion of adjuvant RT [36]. This phenomena is known as chronic fatigue syndrome. The description included requiring a person to experience 6 or more months of chronic fatigue of new or definite onset that is not substantially alleviated by rest, not the result of on-going exertion, and results in substantial reductions in occupational, social, and personal activities [37].

Radiotherapy induced fatigue-Prevention: Anticipation and early recognition of the individual risk for RIF could lead to possible preventive measures, such as prehabilitation instead of rehabilitation. A multimodal, multidisciplinary approach may be necessary to prevent RIF, including psychosocial intervention, physical exercise, and medications to address the contributing factors of RIF. As heme levels seem to have an impact on the incidence of RIF upon completion of EBRT, their stabilization is vital to prevent the worsening of fatigue symptoms during treatment [38]. Patients with increased age and high baseline fatigue levels are at risk of experiencing severe RIF [39].

In 2004 Wratten et al., reported that RIF appeared to plateau between week 4 of treatment and 2 weeks after treatment among patients with early stage BC undergoing adjuvant RT; they found fatigue began to settle by 6 weeks after treatment. In their study, significant fatigue was predicted by a higher baseline fatigue score, red blood cell count, neutrophil count, and D-dimer levels. Baseline fatigue correlated with higher body mass index and altered levels of C-reactive protein, soluble thrombomodulin, tissue plasminogen activator, von Willebrand factor antigen, interleukin-6, ICAM-1, hemoglobin, red blood cells, monocyte, and neutrophil counts. The most predictive factors for RIF in their study were a higher baseline fatigue level and more elevated baseline neutrophils and red blood cell counts. Results of a feasibility study presented in 2018, aiming to evaluate behavioral interventions in early BC patients with RIF, are awaited and they will undoubtedly be of interest in this context [40].

Radiotherapy induced fatigue-treatment approaches: Clinical practice guidelines are available to assist physicians in the management of RIF [41-45]. According to the NCCN, physical therapy and occupational therapy are recommended as the interventions of choice in patients with RIF. The NCCN also recommends psychosocial interventions, such as cognitive-behavioural therapy, psycho-educational therapy, supportive-expressive therapy, nutritional guidance, hygiene, stimulus control, and sleep restriction [46]. Besides the non-pharmaco logic treatment approaches, the NCCN advises the use of psychostimulants, such as methylphenidate and modafinil, after excluding other causes of fatigue like pain, anxiety, depression, anemia, sleep alteration, nutritional factors, and other comorbidities. Non-pharmacologic treatment approaches include laughter yoga, mat pilates, foot bath foot reflexology, music therapy, and polarity therapy [47-52]. During and after RT, patients are recommended to take 150 min of "moderate-intensity exercise" per week (e.g., walking 30 min 5 days per week). Most of these exercises involve range of motion/flexibility, muscle strength, aerobic training, and mind/body fitness [53].

Sleep quality: Sleep is an essential component of overall human health but is so tightly regulated that when disrupted can cause or worsen certain ailments [54]. Despite being used commonly in sleep medicine, the term "sleep quality" has not been rigorously defined. Sleep is a multidimensional construct, often referred to as in terms of its quality. Sleep quality has been a well-recognized predictor of physical and mental health , cognitive status, wellness and overall vitality [55-62].

Sleep quality-effects of its dearth: Chronic sleep deprivation has serious negative impacts on health, quality of life and neuro-cognitive performance [63-67]. Breast cancer patients often complain of sleep problems; it is estimated that the prevalence of poor sleep in breast cancer patients range from 20%-70% [68]. The proportion of sleep disturbances in this population is higher than the observed in healthy adults [69, 70]; and in other oncological patients [71].

Sleep quality-causes: The aetiology of sleep disturbances in breast cancer patients is multi-factorial; in fact, demographic, environmental and lifestyle factors, psychological disturbances and comorbid medical disorders have been pointed to as main factors contributing for its occurrence [72, 73]. Cancer-related treatments, and their wide range of side effects, are other important feature frequently associated with the occurrence of sleep disturbances [74, 75]. In addition, breast cancer diagnosis and associated treatments, may also contribute for worsening pre-existing sleep problems [76].

Sleep quality-circadian regulation: The disturbance of the biological clock in those diagnosed with cancer is evidenced by the alteration of the circadian rest-activity rhythm 46 and the sleep-wake cycle [77]. Circadian disruption in cancer has been unrecognized and overlooked until recently; however, patients with breast cancer experiencing disturbed rhythms have shorter overall survival than others with robust rhythms [78].

Sleep quality-immunity, metabolic regulation: Strong preclinical and clinical evidence exists for the role of inflammatory processes in the development of behavioral symptoms, including sleep disruption and fatigue. Proinflammatory cytokines, such as interleukin (IL)-1β, IL-6, and tumor necrosis factor (TNF)-α, are immune mediators released by activated immune cells in response to pathogen invasion, tissue damage/injury, and cytotoxic factors, including chemotherapeutic agents. Fatigue and sleep problems represent key features of these cytokine-induced behavioral alterations [79-81]. Cancer drugs can enhance pro-inflammatory cytokine release from healthy and/or malignant cells, and high levels of serum cytokines (TNF-α, IL-1, and IL-6) have been associated with chemotherapy-induced fatigue [82-84] Sleep plays an important role in metabolic regulation, and sleep disruption has been linked with weight gain. Overweight is associated with a chronic low-grade inflammatory state characterized by increased levels of inflammatory markers, including C-reactive protein and proinflammatory cytokines [85].

Sleep quality-behavioral factors: The development of sleep disturbance in patients with breast cancer can be understood by using a well-known behavioral model of sleep disturbance, and later refined by Morin [86, 87]. In women with breast cancer, sleep disturbance might occur as a result of having a predisposition for sleep disturbance. Factors that can predispose someone to sleep disturbance include female sex, trait anxiety, and a family history of sleep problems. When women are diagnosed with breast cancer, they experience a myriad of precipitating factors for sleep disturbance. These factors may involve the stress related to the diagnosis of breast cancer, cancer

treatments and the associated side effects, and psychiatric and physical factors, such as anxiety, depression, pain, and frequent urination. Patients might respond to their sleep disturbance by spending more time in bed to compensate for lost sleep, shifting their sleep phase by either delaying sleep or wake time, and taking naps. These behaviors, although initially adaptive for acute short-term illness, are maladaptive for patients who have chronic illness and chronic sleep disruption. 80 Sleep disturbance in breast cancer is often related to psychological sequelae that include depression and fatigue [88, 89]. Psychological stress can have a significant impact on sleep and is a precipitating factor for the development of insomnia. With more than 20% to 30% of women with breast cancer reporting depression, and depression worsening with more-advanced breast cancer, the combination of cancer and depression acts synergistically to hamper sleep [90, 91].

Sleep quality-impact by radiotherapy: Breast cancer treatments have several associated side effects, which may contribute to impaired sleep in these patients. The cumulative effect of toxic agents on body functions, the physical impact of distressing symptoms (including nausea, vomiting, diarrhoea, urinary frequency or skin reactions related with radiotherapy), changes in body image and hospitalization, as well as other comorbid-related conditions (e.g.: pain, fatigue, depression, anxiety, stress), are frequently reported as the main cause or aggravating factor for sleep disturbances in this population [72, 73, 92] Breast cancer patients submitted to radiotherapy tended to report higher levels of sleep disturbances than those not submitted to this type of treatment [93-96]. However, as previously mentioned, when radiotherapy was compared with chemotherapy, lower levels of sleep disturbances were observed [96, 97]. For a better understanding of the relation between breast cancer treatment and sleep disturbances, more prospective studies with baseline evaluations before treatment are needed. In fact, previous studies have shown that women with breast cancer frequently report higher levels of sleep disturbances prior to treatment [98-100] whereas for some patients the onset of insomnia followed the breast cancer diagnosis and others reported that cancer either caused or aggravated their sleep difficulties [76].

Anxiety

Anxiety is a normal emotion. Anxiety is the feeling of fear that occurs when faced with threatening or stressful situations. It is a normal response when confronted with danger, but, if it is overwhelming or the feeling persists, it could be regarded as an anxiety disorder [101]. Most cancer survivors adjust well to life after cancer but some experience persisting negative mood, such as cancer-related fears, posttraumatic stress, anxiety, or depression. Mood fluctuations may not reach criteria for a clinical diagnosis but subclinical symptoms can interfere with quality of life [102]. After cancer treatment, many survivors report feeling alone or even abandoned following the intensive support provided during their treatment. Many survivors experience emotional distress that does not meet the clinical criteria for anxiety disorder.

Anxiety in cancer patients-factors affecting: Nearly half of cancer patients report having a lot of distress. Patients with lung, pancreatic, and brain cancers may be more likely to report distress, but in general, the type of cancer does not make a difference. Factors that increase the risk of anxiety and distress are not always related to the cancer.

The following are risk factors for high levels of distress in patients with cancer:

1. Trouble doing the usual activities of daily living.
2. Physical problems and side effects of treatment (such as fatigue, nausea, or pain).
3. Problems at home.
4. Unmet social and spiritual needs.
5. Depression, cancer-related post-traumatic stress, or other emotional problems.
6. Being diagnosed with advanced-stage cancer.
7. Having experienced childhood abuse.
8. Being younger, female, or non-White.
9. Having a lower level of education.

Patients who have a high level of distress when they are diagnosed with cancer are more likely to have continued high levels of distress after their diagnosis.

Anxiety in cancer patients-symptoms: Symptoms of autonomic over-activity include palpitation and sweating. Anxious behaviours such as restlessness and reassurance-seeking are a feature. Changes in thinking include apprehension, worry and poor concentration, and physical symptoms such as muscle tension or fatigue may occur.

Since anxiety is a frequent response to threat, it is found in all clinical populations. It can be adaptive, but in certain circumstances it becomes maladaptive or morbid. Such pathological anxiety is identified by:

1. Being out of proportion to the level of threat
2. Persistence or deterioration without intervention
3. A level of symptoms which are unacceptable regardless of the level of threat (these include recurring panic attacks, severe physical symptoms, and abnormal beliefs such as thoughts of sudden death)
4. A disruption of usual or desirable functioning

It is difficult to judge when anxiety is disproportionate to the threat of cancer, since the disease is always associated with some real threat. The level of anxiety must be judged against the proximity of threat. For example, it is normal to experience considerable anxiety for a period of 7–10 days after receiving bad news [103], but as the degree of real threat varies throughout the history of the cancer, so therefore do levels of normal anxiety.

Anxiety in cancer patients-diagnosing breast cancer patients: Given the scope of mood problems cancer survivors may experience, clinicians need easy to

administer methods for screening so that they can make appropriate recommendations and referrals. Numerous methods for screening and diagnosing mental health needs in survivors have been validated that balance ease of use and sensitivity and specificity for defining treatment needs.

Anxiety in cancer patients-its impact on effectiveness of radiotherapy: Currently 458000 people live with cancer in the UK [104]. Over 50% of these patients will be managed with radiotherapy, [105, 106] which can cause procedural anxiety, with approximately 49% of patients experiencing anxiety and psychological distress [107, 108]. Procedural anxiety refers to excessive worry or fear of medical procedures [109] and is a phenomenon exacerbated by new developments in radiotherapy, for example, stereotactic and adaptive radiotherapy, that require long treatment times. High levels of distress during radiotherapy can directly impact the accuracy and efficacy of the procedure [110] Procedural anxiety is not limited to radiotherapy and also occurs during diagnostic imaging, and other invasive procedures performed on a conscious patient. Between 2% and 5% of MRI scans are terminated due to procedural anxiety this equates to a significant financial cost [111, 112].

Anxiety in cancer patients: Effect of radiotherapy: Data indicate that cancer inpatients as a group report greater anxiety over the circumstances of hospitalization than inpatients receiving treatment for non-malignant conditions [113].

Radiation therapy patients might therefore report substantial distress at all points of assessment. Second, post-operatively cancer patients report greater and more lasting state anxiety, general feelings of experiencing a crisis, and feelings of helplessness than are reported by general surgery patients [114]. Thus, a general decline in state anxiety for patients undergoing radiation might not be evidenced; instead distress may be maintained or possibly increased when a treatment is over. Third, radiation therapy also differs from many of the surgery and diagnostic procedures studied in that rather than a single episode; most patients undergo repeated radiotherapy treatments. Kendall et al.'s research with cardiac catherization patients and Shipley et al.'s research with endoscopy patients suggest, however, that even patients with non-malignant diseases fail to adapt when undergoing repeated diagnostic procedures [115, 116]. Radiation therapy patients may also not adapt to treatment, and thus be as anxious when anticipating their second treatment as their first.

Depression

Depression is a common and recurrent mental illness with a complicated etiology, but the specific pathogenesis is not clear. Depression is a leading cause of disability, and women diagnosed with breast cancer are at a higher risk of mental illness when compared to the general population. Rapid advances in the understanding of tumor immunology and neuroimmunology have provided new evidence for the pathogenesis of depression. Dysfunction of immune cells and cytokines cause depression by affecting tryptophan metabolism, serotonin levels, and blood-brain barrier permeability. Dysregulation of cytokines or intestinal flora may be shared between patients with depression and breast cancer.

It has also been found to play a critical role of depression/anxiety as an independent factor in predicting breast cancer recurrence and survival. It has been demonstrated that

BC patients have high levels of anxiety, depressive symptoms and lower QoL [117-120]. These alterations in mood in oncological patients can result, furthermore, in non-compliance with treatment, longer hospitalization, wrong prognosis and increased mortality [121-123]. Studies have revealed that the longer the time passed since diagnosis, the higher the levels of S/A and depressive symptoms. We also found a significant relation between severe anxiety and check-up situation. Some studies have reported that when cancer is initially diagnosed, anxiety increases in a natural way, then diminishes with time as the patient adapts to the illness, but that it can increase again at a later point if the symptoms become more serious [124]. The prevalence of depression is high during the first year after breast cancer diagnosis. A study demonstrated in a very large sample of cancer patients that the prevalence of depression among breast cancer survivors was about 32.8%.

Depression in cancer patients - factors affecting: Negative mood symptoms such as anxiety and depression often co-occur. In a population-based, longitudinal study, 9% of survivors had both anxiety and depressive symptoms.

1. In a heterogeneous sample of adult cancer survivors, a diagnosis of melanoma, survivors not in remission, and smoking.
2. Females [61]
3. A higher number of comorbid conditions [36, 63, 74]
4. Negative body image for women [75, 76]
5. Financial problems [64, 71, 77, 78]
6. Within the first 2 years of survivorship [79]
7. Prior history of depression [33, 35]
8. A sedentary lifestyle [33, 35]
9. Loneliness [80]

Longitudinal studies have examined depressive symptoms following a cancer diagnosis. Revealing that most could be classified as having very low or low depressive symptoms while few had consistently borderline scores. Some patients also reported with high depressive scores at first diagnosis which declined over time after treatment was completed. Depression has been found to be associated with a 24% increase in the risk of cancer recurrence and is associated with a 30% increase in the risk of all-cause mortality. Some studies have reported that when cancer is initially diagnosed, anxiety increases in a natural way, then diminishes with time as the patient adapts to the illness, but that it can increase again at a later point if the symptoms become more serious [124]. The time of diagnosis, the course of CT treatment and the months following the end of the treatment are times of bad adaptation to the transition and of fluctuating anxiety [125]. Other studies, however, have found that patients diagnosed with BC felt anxious and depressed, but this tended not to change significantly during the therapeutic procedures [119], and it was found that these symptoms persisted for long periods 126. It has been suggested

that psychological symptoms are a result of both the cancer itself and the harmful effects of its treatment [118].

Nutritional status

Nutrition in cancer is now a topic of acknowledged significance. Traditionally, undernutrition has dictated clinical concerns, although the evidence indicated that 8% to 84% of the patients would suffer from undernutrition throughout the disease course. A clarification of that wide interval was overlooked; nonetheless, recent evidence draws our attention to the increase of excess body weight and obesity in oncology. Robust findings, from recent epidemiological studies, show that obese subjects have higher rates of some forms of cancer [10]. Moreover, once the disease is installed, obese patients have a significantly reduced survival compared with those of adequate weight, and obesity has been consistently associated with cancer recurrence after antineoplastic treatments and/or surgery. In addition, of acknowledgeable relevance is the fact that cancer patients who are of normal weight, overweight, or obese are likely to have depleted muscle mass; this clinical condition has been associated with poorer performance status and decreased survival. Undernutrition and overweight/obesity have distinct implications and bear a negative prognosis in cancer. Repetitive and intensive nutritional counseling is necessary to improve QOL and to prevent deterioration of nutritional status in cancer patients receiving RT.

Progressive deterioration in nutrition in cancer patients is known as tumour cachexia. The clinical picture is characterised by anorexia, loss of weight and poor general status, all of which can lead to the death of the patient. Although the principal clinical characteristics are anorexia and weight-loss, other complex clinical and analytical alterations are produced. These include asthenia, premature satiety, alterations in immune function, muscle atrophy, modifications in body image, anaemia, hypoalbuminaemia, hypolipoproteinaemia, hypertriglyceridaemia and hyperlactacidaemia. The causes of the malnutrition can be diverse, among which are the effects of the tumour, the site of the tumour, the production of specific cytokines and the effects of the anti-tumour therapy administered.

The cachexia–anorexia syndrome occurs frequently in cancer patients; the approximate incidence being 50%. The prevalence of cachexia/weight-loss varies as a function of the phase of the disease 144 and the tumour site. In advanced phases, it is present in up to 80%-90% of the patients, and between 20% and 25% of the cancer patients die directly as a result of the cachexia. Malnutrition/weight-loss is associated with a lower survival, poor response and a decreased tolerance to the anti-cancer therapy. Further, there is a decrease in the patient's general status together with a higher health-care cost and longer hospitalisation. Among the different prognostic factors such as the type of tumour, the stage of the disease, the general status of the patient and the weight-loss/malnutrition, it is the weight-loss/malnutrition that is the most amenable to intervention therapy. Despite the importance of the theme, there have been few large-scale studies assessing the prevalence of malnutrition in patients with cancer, and nutritional status has not been systematically evaluated in standard clinical practice in any of the major centres in India.

Survivors with better nutritional status have been found to have better functioning scales and experienced fewer clinical symptoms. It appears important to provide educational and nutritional screening programs to improve cancer survivor quality of life. The scored PG-SGA is a nutrition assessment tool that identifies malnutrition in ambulatory oncology patients receiving radiotherapy and can be used to predict the magnitude of change in QoL. Nutritional risk and poor performance status were associated with a higher occurrence of death in women with breast cancer. The use of these two indicators improves their predictive accuracy for mortality.

Given the positive effect of the educational-supportive intervention on reducing stress and improving nutritional status, it can be incorporated into training and care programs to improve nutritional status and reduce stress in patients with breast cancer. Malnutrition has a high prevalence in Iranian cancer patients and has a close relationship with mortality, morbidity and treatment-related problems and also quality of life. Therefore, periodical assessment by PG-SGA to detect malnutrition in patients should be made so that appropriate nutritional interventions can be provided. The high prevalence of malnutrition, has been found to be due to the fact that patients presented to treatment at locally advanced or metastatic stages. In order of early detection of situations at risk of malnutrition, the assessment of nutritional status should be an integral part of the overall taken care of patients with breast cancer.

CONCLUSION

Radiotherapy-induced fatigue is a common early and chronic side-effect of irradiation. In BC patients who undergo adjuvant RT, RIF is underreported, underdiagnosed and undertreated. RIF may become a chronic state with subsequent non-compliance, which further compromises treatment efficacy. It is frequently underestimated by medical and nursing staff and its reasons, correlates and prevalence are poorly understood. Knowledge on the therapeutic options in management of radiotherapy-induced fatigue is still limited. It is essential to evaluate patients for their potential risk and to adequately inform them about predisposing factors and treatment options to prevent and treat fatigue. Standardization of the evaluation and assessment tools need to be established to ensure the full reliability of study results. Significant reduction in fatigue, tension, depression and anger has been observed in the out-patients undergoing curative or palliative radiotherapy. Several interventions have been tested in the management of radiotherapy-related fatigue and some randomized studies have been recently published. Although an optimal method has not yet been established, some promising results have been reported with relaxation therapy, group psychotherapy, physical exercise and sleep. Adequate management should involve an early start after cancer diagnosis and before commencing cancer treatment using a multimodal, multidisciplinary approach to prevent high severity. Further methodologically correct studies are warranted to define better the causes, optimal prevention and management of this symptom.

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