

Review Article

Non pharmacological interventions to manage Cancer-related fatigue (CRF) - An overview

ABSTRACT

Fatigue is almost common problem often reported by the cancer patients that severely affects all aspects of quality of life. Prevalence of cancer related fatigue ranges from 50% to 90% of cancer patients overall. After addressing treatable contributing factors, such as hypothyroidism, anemia, insomnia, pain, emotional distress, medication adverse effects, metabolic disturbances, or organ dysfunction such as heart failure, myopathy, and pulmonary fibrosis, patients may be screened with a short fatigue assessment tool. There is a pressure for pharmacologic therapy to shift away from reliance on opioids and ineffective procedures toward comprehensive cancer related fatigue (CRF) management that includes evidence-based nonpharmacologic options. This white paper details the magnitude of the current CRF problem including its impact on quality of life as well as the challenges of CRF management for patients and a healthcare workforce engaging prevalent strategies not entirely based in current evidence. Transforming the current system of CRF care to a responsive comprehensive model necessitates those options for treatment and collaborative care must be evidence-based and include effective nonpharmacologic strategies that have the advantage of reduced risks of adverse events and addiction liability. Clients-Patients with cancer related fatigue may benefit from self-administrable nonpharmacological interventions without any side effects.

The evidence demands a call to action to increase awareness of effective non pharmacologic treatments for CRF, to train health care practitioners and administrators in the evidence base of effective nonpharmacologic practice, to advocate for policy initiatives that remedy system and reimbursement barriers to evidence informed comprehensive CRF care, and to promote ongoing research and dissemination of the role of effective non pharmacologic treatments in CRF, focused on the short and long term therapeutic and economic impact of comprehensive care practices.

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Keywords: [Cancer-related fatigue, Non pharmacological, intervention]

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INTRODUCTION

Fatigue is one of the most common problems often reported by the cancer patients that severely affect all aspects of quality of life.^[1] CRF is the highly prevalent and devastating symptom experienced by many of the cancer patients at diagnosis, which elevate during treatment and often continue for months to years after treatment. It is subjective in nature; fatigue is common in people with cancer, but it's different for each person.^[2] National Comprehensive Cancer Network defines cancer-related fatigue (CRF) as 'a distressing persistent, subjective sense of physical, emotional and/or cognitive

tiredness or exhaustion related to cancer or cancer treatment that is not related to recent activity and interferes with usual functioning'.^[3]

A lot of evidence and research findings on CRF have been provided within the last two decades, still CRF is continued as underreported, underdiagnosed, and undertreated problem. The pathogenesis of cancer-related fatigue is not well explained, and a variety of mechanisms may contribute to the fatigue in cancer [clients-patient](#)^[4] These includes effects of cancer and its treatment on neuropsychological impairment, muscle metabolism dysregulation, circadian rhythms disruption, inflammatory mediators and stress, immune activation, and hormonal imbalance related to effects on the hypothalamic-pituitary axis, early menopause in women, or androgen deficiency in men.^[5, 6,7,8,9]

MAGNITUDE OF THE CRF

Radiation therapy forms a fundamental part of management of a cancer patient. Largely, about 80% of cancer patients require radiation at some point of time either in the form of radical, adjuvant or palliative intent. The radiation treatment is delivered over a period of several weeks in which invariably normal tissues are also exposed. These result in side effects impairing the nutrition, general condition of the patient and enhance the fatigue already present.^[10] Fatigue prevalence surges over the course of radiotherapy.^[11] Unlike simple tiredness or situational fatigue, it is more devastating and severe; less likely to be relieved by simple rest; and may lead to withdrawal from meaningful and enjoyable events and may even lead to discontinuation of treatment.^[12] During the course of radiotherapy, fatigue usually increases, but typically wanes within weeks after the end of radiation treatment.^[13] However, in up to 40% of [clientspatients](#), it can persist long after the completion of therapy.^[14] Similar to radiotherapy a very high percentage of patients who are receiving chemotherapy also experience fatigue.^[15, 16]

POSSIBLE CAUSES OR CONTRIBUTORS TO CANCER-RELATED FATIGUE

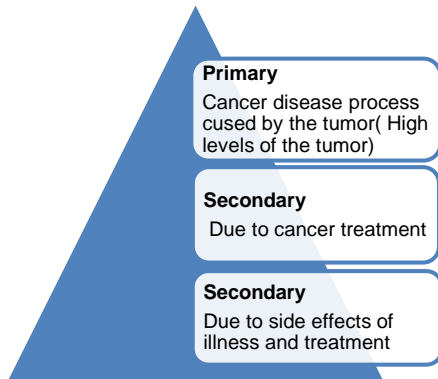


Fig 1- Possible causes or contributors to cancer-related fatigue

Underlying etiology and risk factors for CRF are not fully known.^[17] Studies have identified risk factors which are associated with cancer related fatigue. It may be the cancer and/or the cancer treatment. Fatigue is often caused by more than one factor. Commonest causes of cancer-related fatigue are: anemia, pain, emotional distress, sleep problems and drugs.^[18]

IMPACT OF CRF ON QUALITY OF LIFE

Cancer therapy-related side effects include: chest pain, nausea or vomiting, oral infections, diarrhea, constipation, fever, exhaustion, loss of appetite, difficulty to breathe, dermatitis, sensory or motor problems, hemorrhage, palmar-plantar syndrome, pain, bruising and other rare side effects.^[19] The presence of any one or a combination of these side effects can have a detrimental effect on one's overall well-being, body image, and self-perception.^[20] The impact of CRF on physical, psychosocial, and economic and occupational domains was evaluated in the year 2000 in Fatigue Coalition follow-up survey. In this survey eighty percent of the respondents were reported decreased energy levels and a feeling of tiredness. The survey also sought to clarify the psychosocial effects of cancer therapy. Decreased overall motivation, needing to push oneself, and feeling sad, frustrated, and irritability are most commonly reported symptoms by the cancer patients, cognitive function was also affected; manifested as decreased concentration, decreased memory, and difficulty keeping dates straight. Patients who still employed were absent from work 4.2 days per month during and after treatment had ended. The potential economic impact of fatigue is considerably high;75% of patients and 40% of caregivers are

forced to change their employment status due to cancer-related fatigue.^[21] Another study about employment participation in early-breast cancer patients further highlighted the enormous socioeconomic impact of fatigue by showing that fatigue patients were more likely to experience diminished employment after 2 years of follow-up.^[22] [PatientsClients](#) identified the certain activities as the most difficult; walking distances, doing household tasks, cleaning the house, socializing, and cooking food.²¹ A research study also revealed that CRF is an independent causative factor for dissatisfaction of [client-patient](#) with life. Those individuals reporting fatigue levels in the severe range (7–10/10) were least likely to feel satisfied with life (odds ratio 0.28, 95% confidence interval: 0.09–0.91, $P=0.03$).^[23]

Table1-The impact of fatigue: outcomes of a survey by the Fatigue Coalition ^[21]

Physical impact	Financial impact	Social and emotional impact
Difficulty in carrying out tasks -56%	71% of clientspatients lost one or more days of work	59% reported difficulty in mingling with friends and family
Difficulty in climbing stairs -56%	31% lost a complete week of work	37% had difficulty in preserving relationships
Difficulty in walking long distances- 69%	28% had to stop working	30% found difficult to have intercourse with spouse
Difficulty in continuing exercise- 67%		

NON-PHARMACOLOGICAL APPROACHES (COMPLEMENTARY THERAPIES) FOR MANAGEMENT OF CANCER-RELATED FATIGUE

Most of the nonpharmacological approaches are considered for some extent as they improve overall wellbeing of the [clientspatients](#). Small sample studies involving yoga, acupuncture and acupressure, massage, healing touch and aromatherapy, foot soak with reflexology has demonstrated promising results in relieving fatigue. Further intervention studies with higher statistical power are required to develop a larger body of evidence with more applicable conclusions.^[24]

Few common non-pharmacological approaches either as a single therapy or in combination used in the management of cancer-related fatigue, which can be self-administered after a brief training or education, accepted and affordable by the [clientspatients](#) are;

- Exercise
- Nutrition and hydration
- Acupressure and
- Yoga and
- psychosocial interventions

EXERCISE

There is growing evidence which provides a strong indication that exercise is advantageous to cancer [clientspatients](#). Exercise during and after cancer treatment has been shown to be safe and sound to reduce fatigue, increase physical fitness and enhance the health-related quality of life. Aerobic exercise significantly reduces fatigue; however, the role of resistance training and alternative forms of exercise are less clear.^[25] Exercise is likely to play an effective role in managing the side effects of CRF such as cognitive impairment, sleep disturbances, depression, pain, anxiety and physical impairment including defective muscular function, cardio-pulmonary function and bone mass. It can be tailor-made to the precise needs of each cancer client or survivor.^[26, 27, 28]

Exercise helps to produce endorphins, a chemical secreted in the brain that act as natural analgesic and also helps to induce sleep which in turn helps to reduce stress. Conventional wisdom holds that a workout of low to moderate intensity makes one to feel energized and healthy. Researchers found that [clientspatients](#) those who have participated regularly in aerobic exercise had reduction in level of stress, stabilized mood, improved sleep, and improvement in self-esteem. Five minutes of aerobic exercise also can contribute to anti-anxiety effects.^[29]

All forms of exercise are recommended to help decrease fatigue, but the more aerobic the activity the better, e.g., walking, swimming, cycling, running, rowing. Interval training is best for physical and psychological benefit which means that the

exercise should be rhythmic, involve repetitive movements of large muscle groups, include a series of short, intensive periods, be at a moderate intensity (60-85% of estimated maximum heart rate), ideally done several times a week and sustained. The exercise should be progressive. A daily record or exercise diary can be very helpful to set realistic goals, record progress and help motivate the individual toward helping themselves to reduce their fatigue.^[30]

Precautions to be taken by anyone taking up this approach would be:

- No lifting of heavy weights following lymph node surgery
- Recent vomiting
- Chemotherapy within previous 24 hours
- Confusion, pallor, blurred vision, fever, chest pain, dizziness, sudden shortness of breath, irregular pulse
- Current viral infections
- Pain.^[31,32]

ACUPRESSURE

Acupressure is a component of traditional Chinese medicine that uses pressure via finger, thumb or a device to stimulate specific acupoints for therapeutic purposes and stimulating these points can correct imbalance between *Qi* (*Qi* is a vital energy of life) via channels and subsequently treat the diseases. Balancing of *Qi* helps to attain therapeutic supports by improving the physiological functions.^[33, 34, 35] Biochemical mechanism of acupressure describes the stimulation of specific acupoints along the meridian leads to complex neuro-hormonal responses. It involves the counteraction among hypothalamic-pituitary-adrenocortical (HPA) axis that leads to overrun of cortisol and cause a relaxation response. Also, it modulates the physiological response by increasing endorphin and serotonin transmittance to the brain and specific organs through nerves and meridians.^[36]

As per the Meridian theory, on stimulation of acupoints, the area along the meridian will be affected whereas activating proximate acupoints would affect the functioning of local tissues. Acupressure mediates nitric oxide (NO) signal, known to improve local microcirculation via cyclic guanosine monophosphate (cGMP). It helps in enhancing the physical performance by suppressing fatigue-inducing molecules in the blood.^[37] Several randomized controlled trials of acupressure to reduce fatigue in patients with cancer have been conducted. In these studies, acupressure has been administered by a traditional Chinese medicine provider; self-administered; delivered as auricular acupressure; or combined with other therapies such as aerobic exercise, essential oils, and education.^[38, 39, 40, 41] Acupressure has been shown to be safe and acceptable by patients with cancer.^[33, 34, 35] Also, acupressure appears to affect significant improvements, on the order of 30% to 40%, in fatigue severity.^[42]

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NUTRITIONAL THERAPY

There are various reasons for developing nutritional complications in cancer patients which contributes to the cancer related fatigue.^[43] The systemic nature of cancer promotes metabolic dysregulation and increased catabolism or even cachexia.^[44,45,46] Adverse effects of drugs including altered taste, anorexia, unintentional weight loss, xerostomia, nausea and vomiting and eventual malnutrition in some cases, increased adiposity or obesity.^[47] Sarcopenic obesity may lead to greater loss of functionality, lower quality of life and greater mortality risk compared to cachexia or obesity alone. Breast cancer patients experience unintentional weight gain due to the effects of chemotherapy, endocrine treatment and/or postmenopausal status. Chronic low-grade inflammation, as seen in obesity, is considered a factor in the development of CRF.^[48]

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Nutrition Strategies to manage fatigue are:

- Select balanced meals and snacks
- Eating every three hours to keep energy levels up. Each meal and snack must contain a source of complex carbohydrates, protein and healthy fats to give sustained energy. Whole grains, sweet potatoes and other fiber-rich foods must be chosen for complex carbohydrates. They provide a continuous supply of energy.
- Sources of protein consist of fish, chicken, meat, dairy products, nuts, seeds, beans and lentils. Protein-rich food must be added at all meals and snacks to keep energy levels up and to preserve muscle.
- Healthy fat such as avocado, olive oil, nuts and seeds must be comprised with each meal and snack. This will give a constant supply of energy.
- Whole grains, fruits and vegetables, beans, peas, lentils, nuts and seeds contain adequate fiber.

- Vegetables and fruit are excellent sources of phytochemicals, antioxidants and vitamins that protect healthy cells help fight cancer cells, lower inflammation and boost immune system.
- Fish such as salmon, mackerel, sardines and Arctic char are rich in omega-3 fatty acids which lower inflammation
- Need at least 2 liters of fluid each day. ^[49]

YOGA

The traditional Indian form of yoga encompasses several domains including ethical disciplines, physical postures, and spiritual practices, with the goal of uniting the mind, body, and spirit for health and self-awareness. ^[50] There are a variety of types of yoga but the most common form adopted by **western society** consists of three basic components; asanas (physical poses), pranayama (breath control), and dhyana (meditation). Specific postures are performed to help improve flexibility and strength, controlled breathing intends to increase focus and relaxation, and meditation aims to relax the mind. ^[51, 52] Yoga tailored for cancer patients aims to be a gentle practice that appropriately accommodates the needs of the **clients/patients**. For patients, approval from an oncologist is needed before beginning the practice, and instructions are modified as needed to accommodate each individual patient's needs. Research directs that yoga can produce invigorating effects on physical and mental energy, which are similar to some of the effects of aerobic exercise, and thereby may contribute to reduce level of fatigue. ^[53]

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PSYCHOSOCIAL INTERVENTIONS

Psychologically based interventions include methods that focus on cognition, coping skills, and behavior. Psychological interventions such as cognitive-behavioral therapy (CBT) aim to influence or change cognitions, emotions, behaviors or a combination of these. ^[54] Interventions which target these processes may improve symptom management in CRF. ^[55] These therapies may increase knowledge, improve emotional adjustment and enhance quality of life, and have also been associated with improved coping skills, physical health and functional adjustment. ^[56, 57] Patients and healthcare professionals have been reported to have high expectations of, and relatively positive attitudes towards psychological therapies. ^[57] Studies also report that psychosocial therapies are effective in managing the fatigue of patients undergoing treatment for cancer. ^[54]

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Model of Nonpharmacological management of Cancer Related Fatigue (Fig-2)

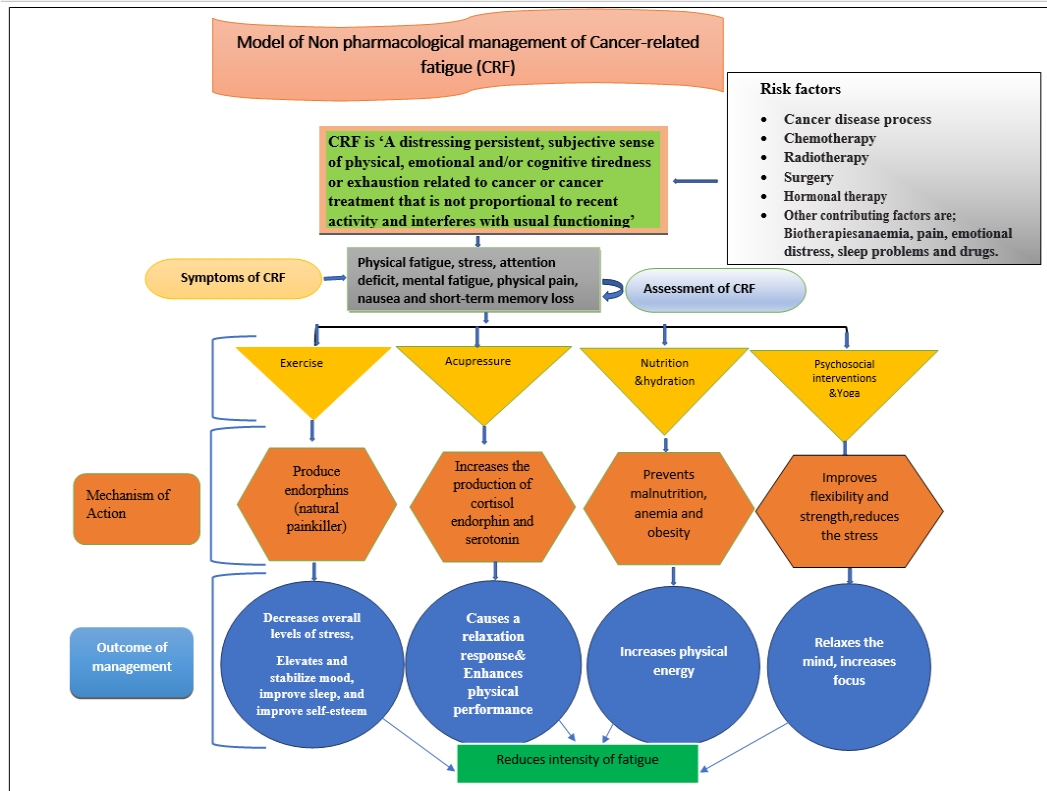


Fig 2: Model of nonpharmacological management of cancer related fatigue

Conclusion:

Cancer-related fatigue is the most prevalent symptom of cancer, reported in 50%–90% of patients and severely impacting quality of life and functional capacity. The condition remains under-recognized. Guidelines suggest screening for fatigue at the initial visit, when the diagnosis of advanced disease is made, and at each hospital visit, as well as the identification of treatable contributing factors. Nonpharmacologic measures that have shown promising results to reduce CRF include exercise, acupressure, nutritional counseling, yoga, psychological interventions and perhaps sleep therapy. Many other modalities may be beneficial and can be used on an individual basis, but insufficient evidence exists to promote any one treatment. Systematic reviews reveal that combinations of nonpharmacological therapies are likely to be the best approaches in management of CRF.

Comment [Ma7]: Give conclusion in light of references mentions on therapies and support your conclusion with studies related to CRF

ETHICAL APPROVAL

Not applicable

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