

Cancer Related Fatigue amongst Patients with Gynecological Malignancies Receiving Various Therapies: An Institutional Experience

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Abstract : Purpose: To find out the prevalence of cancer related fatigue (CRF) and its impact on quality of life (QoL) amongst gynecological cancer patients receiving radiotherapy (RT), chemotherapy (CT) or concurrent chemo-radiation (CCRT). **Material and Methods:** This study included 194 gynecological cancer patients receiving RT, CT, or CCRT who fulfilled the inclusion and exclusion criteria. The CRF was assessed using Brief Fatigue Inventory (BFI) and QoL was measured using Functional Assessment of Cancer Therapy-General (FACT-G) scale. **Results:** Severe fatigue was more prevalent in patients receiving CT (86.66%) and CCRT (64.8%) as compared to RT (37.5%). Moderate correlations were exhibited between CRF due to RT and QoL ($r = -0.747, P < 0.01$), and CCRT and QoL ($r = -0.591, P < 0.01$), whereas weak correlation was found between CRF due to CT ($r = -0.311, P < 0.01$). **Conclusion:** Severity of CRF was more in CT and CCRT patients while QoL was affected more after RT. CRF is a common and often underestimated distressful phenomenon. Adequate attention should be given from the beginning of treatment to improve the QoL of cancer patients.

Keywords: Fatigue, gynecological cancer, quality of life, Brief Fatigue Inventory, FACT-G

Date of Submission: 25-05-2018

Date of acceptance: 09-06-2018

I Introduction

The definition of Cancer Related Fatigue (CRF) as given by National Comprehensive Cancer Network version 2.2017 is “a distressing, persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning”. It is a very common symptom affecting about 80% of cancer patients receiving any type of anti-cancer treatment. ^[1] CRF has a negative impact on patients' well being and QoL. Despite the high prevalence of CRF and its potential negative impact on patients' QoL and emotional well-being, research in this area is still lagging behind and there are only a few studies available in the literature for Indian population. ^[2]

CRF is believed to be multifactorial and the causes include the cancer itself and its treatment, anemia, infection, sleep rhythm disturbances, immune activation, pain, psychosocial factors and so on. Various validated tools are available for the measurement of fatigue but there is no gold standard. The Brief Fatigue Inventory (BFI) is used as screening tool for fatigue which measures severity of fatigue over the previous 24 hour. The BFI has nine items, with the items measured on 0-10 numeric rating scales. ^[3] Functional Assessment of Cancer Therapy-General (FACT-G) is an easy to administer questionnaire widely used to measure health-related QoL in cancer patients.

II Material And Methods

A total of 194 cancer patients were selected for this study. The inclusion criteria was as follows: patients with age more than 18 years and less than 70 years, Eastern Cooperative Oncology Group Performance Status (ECOG PS) 0 to 2, Hemoglobin levels >10gm/dL, patients able to give informed consent. The Exclusion criteria were any patient with known history of psychiatric disorders, neurological impairments, cognitive/perceptual impairments and patients with severe comorbidities. The data was collected from October 2017 to March 2018. Subjects were asked to fill the questionnaire to measure their level of fatigue and QoL by using BFI and FACT-G, respectively. The participants were explained about the questions in their mother tongue and response was noted.

Functional Assessment of Cancer Therapy-General (FACT-G): The latest version 4 consists of a total of 27 Likert-type items formulated into separate subscales: Physical (seven items), emotional (six items), social/family (seven items), and functional (seven items) well-being. Subjects are asked to respond to each item

with a score of 0-4, where 0 = not at all, 1 = a little bit, 2 = somewhat, 3 = quite a bit, and 4 = very much. A higher score indicates a better quality of life. [4,5]

Brief Fatigue Inventory (BFI): In BFI, patients are asked to rate the severity of their fatigue at its "worst," "usual," and "now" during normal waking hours, with 0 being "no fatigue" and 10 being "fatigue as bad as you can imagine." Six items assess the amount that fatigue has interfered with different aspects of the patient's life during the past 24 hours. The interference includes general activity, mood, walking ability, normal work, relations with other people and enjoyment of life. The interference items are measured on a 0-10 scale, with 0 being "does not interfere" and 10 being "completely interferes." Fatigue was categorized using the BFI as either severe (score 7-10) or not severe (score 0-6), with the latter further subcategorized into moderate (score 4-6) and mild (score 0-3). [6]

Statistical analysis: All statistical analyses were performed using SPSS for windows, version 20.0 (IBM Corp., Armonk, New York, USA). In all calculations, the significance level was taken as 0.05. Prevalence rate was measured on the basis of number of patients under the category of mild, moderate and severe and their percentage is calculated from the total number of patient in each of three groups, i.e., radiotherapy, chemotherapy, and concurrent chemo-radiation using the descriptive statistics. Pearson product moment correlation was used to find out the association between the CRF and QOL in the all three groups.

III Results

Patient characteristics like the details regarding age, ECOG PS, concurrent disease and location of cancer for various patients receiving anticancer treatment is given in Table 1. Table 2 describes the prevalence of CRF among the patients receiving various therapies. Out of 24 patients who received RT, 8.33% reported no CRF, 20.83% mild CRF, 33.33% moderate CRF, and 37.5% severe CRF. Among those who received CT, 6.66% reported mild and moderate CRF, while overwhelming majority of 86.67% patients reported severe CRF. Among patients who received CCRT, 8% patients reported mild CRF, 27.2% patients reported moderate CRF and 64.8% patients reported severe CRF.

The mean and standard deviation for the level of present CRF (Q1), usual level of CRF in past 24 hours (Q2), and the worst level of CRF in past 24 hours (Q3) in RT group were 5.21 ± 2.943 , 5.09 ± 2.875 , and 5.15 ± 2.954 , respectively. The mean and standard deviation for the level of present CRF (Q1), usual level of CRF in past 24 hours (Q2) and the worst level of CRF in past 24 hours (Q3) in CT group were 6.51 ± 2.324 , 6.87 ± 2.097 , and 6.92 ± 2.014 , respectively. The mean and standard deviation for the level of Present CRF (Q1), usual level of CRF in past 24 hours (Q2) and the worst level of CRF in past 24 hours (Q3) in CCRT group were 5.632 ± 2.791 , 5.602 ± 2.658 , and 5.607 ± 2.768 , respectively.

Correlation analysis of CRF and QoL revealed negative correlation which meant that the more the increase in severity of the level of CRF, the worst the QoL. The correlation was interpreted separately for CRF occurring due to RT, CT, and CCRT with QoL domains. There is moderate correlation ($r = -0.747$ at 0.01 significance) between CRF due to RT and QoL shown in Table 3 and Figure 1. Correlation between CRF due to CT and QoL reveals weak correlation ($r = -0.311$ at 0.01 significance). Correlation between CRF due to CCRT and QoL revealed negative and moderate correlation ($r = -0.591$ at 0.01 significance).

IV Figures and Tables

Table 1 Patient and disease characteristics.

Characteristics	RT	CT	CCRT
Age (median, years)	54	52	46
ECOG PS			
0	-	-	2
1	11	16	49
2	13	29	74
Cancer site (Total)			
Cervix (131)	7	14	110
Uterus (21)	13	1	7
Ovary (29)	0	29	0
Vagina (9)	3	1	5
Vulva (4)	1	0	3

Table 2 Distribution of CRF

Treatment	Number of patients (n)	No fatigue n (%)	Mild fatigue n (%)	Moderate fatigue n (%)	Severe fatigue n (%)
RT	24	2 (8.33%)	5 (20.83)	8 (33.33)	9 (37.50)

CT	45	-	3 (6.66)	3 (6.67)	39 (86.66)
CCRT	125	-	10 (8)	34 (27.2)	81 (64.8)

Table 3 Correlation between CRF and QoL

Treatment	No of patients	Correlation coefficient (R)	P-value
Radiotherapy	24	r = -0.747	<0.01
Chemotherapy	45	r = -0.311	<0.01
Concurrent chemo-radiotherapy	125	r = -0.591	<0.01

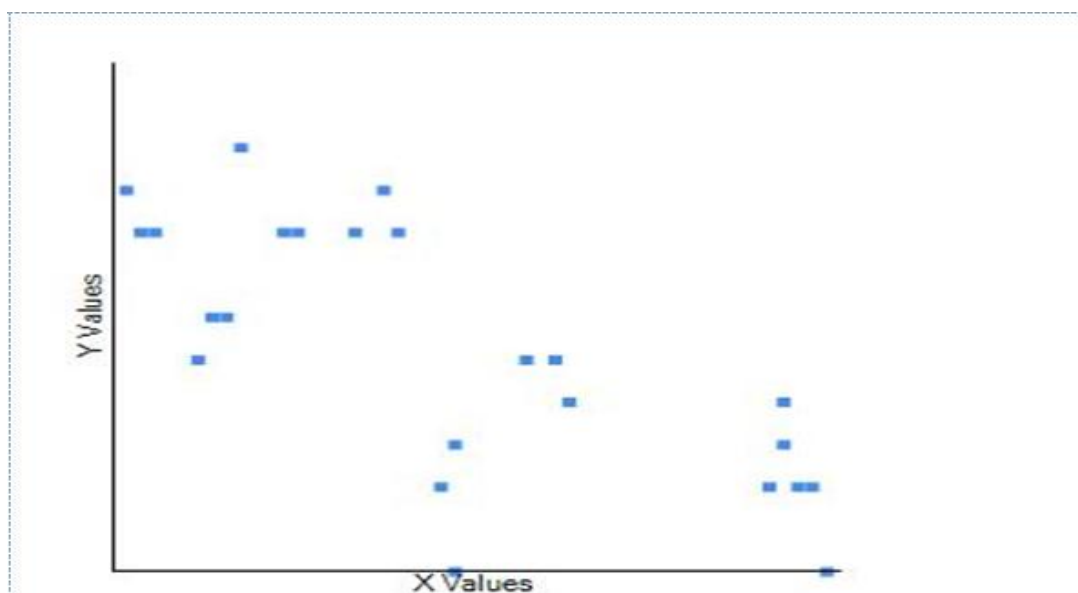


Figure 1 Correlation of fatigue due to Radiotherapy and Quality of Life (QoL) (r = -0.747 revealing strong negative correlation)

V Discussion

CRF is a common phenomenon in individuals with cancer who receive RT, cytotoxic CT, either separately or concurrently. [7] It is a multi-factorial, multidimensional phenomenon, which consists of physical, psychological, social, cognitive, and behavioral aspects. [8, 9] In spite of growing evidence regarding CRF occurring due to various anticancer treatments and how CRF affect patient's QoL, determining its severity is underestimated. The current study stressed on measuring the prevalence rate of CRF (and its severity) among the gynecological cancer patients receiving various anticancer therapies, and how it impacts the QoL.

RT causes transient increase in CRF which accumulates over weeks. It comes back to the pretreatment level at one month post completion of the treatment. CRF during RT is unique as the treatment is stretched over many weeks. CRF is measured in the third week of RT treatment. This is also associated with significant acute radiation side effects which may alter the patient's nutrition, blood parameters leading to aggravation of CRF. [10] Furthermore, RT related CRF starts increasing from second week onwards coinciding with the beginning of RT reactions. This may explain the reason for lesser level of CRF in the present study as the CRF measurement was taken only once, during the third week of RT.

CRF is one of the most prevalent side effects during cancer CT. It usually persists for more than two weeks. [2] It has been observed that during the first 24 to 48 hours of CT, there is a spiked rise in CRF levels. [11,12] CRF level was measured here when the patients were receiving the second or third session of CT treatment. In the present study, among 45 patients who received CT, 39 patients experienced severe level of CRF. So the magnitude of CRF after CT was more than that of RT treatment.

Furthermore, patients receiving a combination of CT and RT, i.e. CCRT, have reported higher levels of CRF compared to those receiving either therapy alone. [13,14] In the present study, among the 125 patients receiving CCRT, 8% reported mild CRF, 27.2% documented moderate level of CRF, and 64.8% reported severe level of CRF. So the magnitude of CRF resulting after CCRT is more than that of RT alone but a little bit lesser than that of CT alone in the present study.

Schmidt *et al.* [15] also found that CRF level substantially increased during CT and RT and among the patients who received both therapies it was 61.4% higher, 30% same, and 8.6% lower CRF level during CT. The present study also documented that the severity of CRF was more in patient receiving CCRT and CT as

compared to those who received the RT alone. Another study also proved that even before the start of their initial treatment, women in the CCRT group reported significantly more CRF, both in terms of severity and disruptiveness, than women in the RT group.^[16]

Correlation analyses of the present study suggested that there is moderate correlation ($r = -0.71$ at 0.01 significance) between CRF due to RT and QoL. At the same time, correlation between the CRF due to CT and CCRT and QoL reveals weak correlation ($r = -0.361$ at 0.01 significance, $r = -0.453$ at 0.001 significance, respectively). But the severity of CRF was found more in CCRT and CT group compared to the RT group. Dagnelie *et al.*^[17] found in their study that the CRF showed by far the strongest univariate correlation with overall QoL ($r = -0.76$, $P < 0.001$). While addressing the issue of CRF, we need to consider the issue from both the patients' and clinicians' perspective. Patients usually do not complain of symptoms of CRF even if it is severe.^[1] This can be circumvented by taking proper history and encouraging patients to share their psychosocial problem with the physician besides the physical complaints. The physician should be trained regarding the use of non-pharmacological therapies such as cognitive behavior therapy, graded exercise therapy, pacing besides the use of pharmacological management like antidepressants and psycho stimulants. Furthermore, a patient and compassionate approach would greatly help to address this issue.

VI Conclusion

Severity of CRF was more in CT and CCRT patients while QoL was affected more after RT. CRF is a common and often underestimated distressful phenomenon. Adequate attention should be given from the beginning of treatment to improve the QoL of cancer patients.

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Shantanu Sharma." "Cancer Related Fatigue amongst Patients with Gynecological Malignancies Receiving Various Therapies: An Institutional Experience." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, vol. 17, no. 6, 2018, pp 77-80.