

Fatigue Assessment during Breast Cancer Radiotherapy

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Abstract

Objective: The objective of this work is to assess fatigue and its impact on the daily life of patients undergoing post-operative radiotherapy for breast cancer.

Patients and Methods: Fatigue was assessed during radiotherapy in patients treated for non-metastatic breast cancer, at the radiotherapy department of the Habib Bourguiba University Hospital in Sfax, Tunisia. The validated Arabic version of the "Multidimensional fatigue Inventory" was used. Fatigue assessment was also done in a group of witnesses.

Results: 50 patients of average age 50 were included, 77 witnesses of average age 45 responded to the questionnaire. All the patients described a feeling of fatigue with variable score. The total fatigue score was 27 to 81 and an average of 51.32. The means of the scores of the different dimensions of fatigue were 10.22 for general fatigue, 11.22 for physical fatigue, 10.78 for reduced activity, 8.5 for reduced motivation and 10.6 for mental fatigue. The number of patients with a total score greater than or equal to 50 was 21 (42%). These scores were lower than those of the witnesses group, and higher than those of the workers of witnesses group.

Conclusion: During radiotherapy for breast cancer patients have a high fatigue score which predominates in the physical and mental dimension while the motivation is not altered. To attribute this fatigue to radiation, other studies are needed to assess fatigue before, during and after radiotherapy, possibly in different institutions with a standardization of the means of evaluation.

Keywords: Fatigue; Breast Cancer; Radiotherapy

Introduction

Fatigue is a very common symptom in oncology, especially during specific treatments [1,2]. Fatigue is a subjective symptom synonymous with weakness or lack of energy [3]. It is a multi-causal subjective experience, as it involves physical, cognitive and emotional aspects [4]. This can be unpleasant and limit daily activities [5]. To this fatigue linked to cancer is added the effect of different specific cancer treatments such as surgery, chemotherapy and radiotherapy [5].

Five dimensions of fatigue were postulated based on the manners in which fatigue can be expressed. Firstly, fatigue can be expressed by general remarks of a person concerning his or her functioning, for example "I feel rested". Secondly, by referring to physical sensations, related to the feeling of tiredness. Thirdly, by referring to cognitive symptoms, such as having difficulty concentrating [1,6]. These three dimensions are labelled general, physical and mental or psychic fatigue. Fatigue can also be expressed by reduced activity and or reduced motivation [1,6].

Healthcare workers are confronted daily with complaints of low energy, weakness, difficulty carrying out physical efforts or intellectual activities [2]. These complaints are verbalized in several ways, all expressing different dimensions of fatigue [1,2,6].

Fatigue can affect patients' quality of life more than pain [7]. Despite its importance, this symptom is underestimated. Few studies have evaluated its frequency, especially during adjuvant treatment for cancer [5,7].

It is reported in 90% of patients in a Tunisian cohort of 40 patients followed in the radiotherapy department of the Salah Azaiz institute in Tunis during the period 2010 - 2011 [7]. But we do not have any objective evaluation of fatigue during radiotherapy for breast cancer in Tunisia and in the Arab world. It is also not known whether fatigue is greater or not in cancer patients compared to the general population.

In order to quantify fatigue, several scales have been described [8,9]. The "Functional Assessment of Chronic Illness Therapy Fatigue" or the FACIT-F questionnaire (version 4), has been used by some authors and consists of assessing physical well-being (7 questions), social and family well-being (7 questions), emotional well-being (6 questions), functional well-being (7 questions) and fatigue (13 questions) [9]. The EORTC scale "EORTC QLQ-C30" is validated for the cancer patient population for the evaluation of quality of life [2,6,9].

Scales, more specific to fatigue, measuring it in a multidimensional way are preferred [6,9]. Among them the "Multidimensional Fatigue Inventory" (MFI-20) assessing the different facets of fatigue: general, physical, sensory, cognitive, and psychological [2,6,9].

The MFI questionnaire has been specifically used for radiotherapy patients [2,8]. It is also the only multidimensional scale measuring fatigue that has been translated and validated in an Arabic-speaking population, by a well-conducted comparative prospective clinical study [6].

The Arabic version of the MFI was validated by Wafaa E., *et al.* in a study of 200 Egyptian Arabic-speaking patients [6]. This study did not include patients undergoing irradiation.

Objective of the Study

- The first objective of this work is to assess fatigue and its impact on the daily life using the Arab version Mfi 20 in patients undergoing post-operative radiotherapy for breast cancer at the Habib Bourguiba Hospital in Sfax (Tunisia).
- The second objective of this study is to compare fatigue in patient group and in a group of witnesses in order to try to find a cause for fatigue.

Patients and Methods

Subject of the study

Presentation of the study

This is a descriptive cross-sectional study carried out at the radiotherapy department of Habib Bourguiba Hospital and University center in Sfax (Tunisia) from June 2018 to June 2019. This work assessed fatigue in patients with non-metastatic breast cancer during adjuvant radiotherapy. Fatigue was also assessed for a control group of women without cancer.

Target population

Patients treated for non-metastatic breast cancer were included in this study. The witnesses are women who do not have cancer and meet the same non-inclusion criteria as the patient.

Patient inclusion criteria's:

These criteria's were:

- A female gender

- Non-metastatic breast cancer
- Patient undergoing adjuvant radiotherapy: women who have had surgical treatment (breast preservative or mastectomy and axillary node dissection) with or without chemotherapy and or hormone therapy and or targeted therapy.

Criteria for non-inclusion:

- Women with anxiety or depression problems (mentioned in the medical record) were not included.
- History of other cancer.

Study instrument

All the patients answered the questionnaire in the presence of the same physician.

Patient fatigue assessment was offered to patients during a follow-up consultation at the 3rd week of radiation therapy. The patients agreed to answer the Arabic version of the "Multidimensional fatigue Inventory: MFI 20" [3]. The witnesses answered the same questionnaire.

It includes 20 questions spread over 5 items: general fatigue, physical fatigue, decrease in activity, decreased motivation and psychic fatigue [3].

These items cover the different aspects in which fatigue can be expressed. Each answer is scored on a scale of 1 to 5 points. The score of each item varies between 4 and 20, the total fatigue score is obtained by the sum of the points. It varies between 20 and 100.

Statistical analysis

The results were analyzed using Excel software. The data were described by percentages for the qualitative variables and by means for the quantitative variables.

Results

Characteristics of the patients

Fifty patients undergoing adjuvant radiotherapy for non-metastatic breast cancer had agreed to answer the fatigue questionnaire.

The average age of the patients was 50 years (30 to 70 years). The women did not have anxiety or depression (mentioned in the medical history) or history of other cancer. A quarter of the patients had a profession. All these patients were on sick leave during radiotherapy treatment.

Characteristics of witnesses

Seventy-seven women (77) agreed to answer the fatigue questionnaire.

The average age of women was 44 (28 to 80). The women did not have anxiety or depression problems (mentioned) or a history of cancer. Women had a trade or attended university in 79% of the cases.

Evaluation of fatigue in patients undergoing radiotherapy

All the patients described a feeling of fatigue with variable score. The general fatigue score varied from 4 to 20. The physical fatigue score varied from 4 to 19.

The drop in activity score also varied widely from 4 to 20. For the decrease in motivation, the score varied from 4 to 16. Psychic fatigue had a score of 4 to 19. The total fatigue score ranged from 27 to 81 and averaged 51.32.

The means of the scores for the different dimensions of fatigue are detailed in table 1.

Dimension	Score
General fatigue	10,22
Physical fatigue	11,22
Decrease in activity	10,78
Decreased motivation	8,5
Psychic fatigue	10,6

Table 1: Averages of scores for the different dimensions of fatigue.

The highest average was for physical fatigue, followed by mental and general fatigue (Table 1). The percentages of patients who had an item score greater than 10 was 60% (30 patients) (Table 2).

Item	Number of patients and % of scores ≥ 10
General fatigue	19/30 (3,3%)
Physical fatigue	22/30 (73,3%)
Decrease in activity	17/30 (56,6%)
Decreased motivation	11/30 (36,6%)
Psychic fatigue	19/30 (63,3%)

Table 2: Percentage score of > or = 10 based items.

The number of patients with a total score greater than or equal to 50 was 21 (42%).

The percentage of patients with a total score greater than or equal to 70 was 13.3%.

The medians for the fatigue scores are as follows:

- General fatigue: 11
- Physical fatigue: 12.5
- Decrease in activity: 10
- Decreased motivation: 8
- Psychic fatigue: 11
- Total median fatigue score: 52.

For the impact of fatigue on the daily life of patients, we noticed that the activities of patients during irradiation decreased with a median score of 10. However, the motivation of patients is the least affected.

Evaluation of fatigue in women in the control group

All of the women in the control group described a feeling of fatigue with a variable score. The general fatigue score ranged from 4 to 15. The physical fatigue score varied from 4 to 16.

The drop in activity score also varied widely from 4 to 20. For the decrease in motivation, the score varied from 4 to 10. Psychic fatigue had a score of 4 to 19.

The total fatigue score ranged from 20 to 80 and averaged 59.38. The means of the scores for the different dimensions of fatigue are detailed in table 3.

Dimension	Score
General fatigue	11,35
Physical fatigue	11,29
Decrease in activity	14,52
Decreased motivation	8,07
Psychic fatigue	14,15

Table 3: Averages of scores for the different dimensions of fatigue.

The highest average concerned the drop in activity, followed by mental and general fatigue (Table 3). The percentages of women who had an item score greater than 10 was 70% (Table 4).

Item	Percentage of women with scores ≥ 10
General fatigue	55
Physical fatigue	40
Decrease in activity	68
Decreased motivation	15
Psychic fatigue	58

Table 4: Percentage of score > or equal to 10 depending on the items.

The number of women with a total score greater than or equal to 50 was 45.

The percentage of women with a total score greater than or equal to 70 was 16%.

The medians for the fatigue scores are as follows:

- General fatigue: 11.5
- Physical fatigue: 11
- Decrease in activity: 13.5
- Decreased motivation: 8
- Psychic fatigue: 12
- Total median fatigue score: 55.5.

For the impact of fatigue on the daily life of the patients, we noticed that the activities of the women in the control group decreased with a median score of 13.5. However, patient motivation is the least affected.

Comparative study

Comparative study of the characteristics of the participants in the study

The comparison of the characteristics of the patients and the controls showed a difference in terms of age and professional activity (Table 5).

Group of women	Middle age (years)	Professional activity	History of cancer	History of psychic disorders
Patients	50	25 %	Breast cancer	0
Witnesses	45	79 %	0	0

Table 5: Comparison of characteristics of women.

Comparative study of fatigue

Comparative study of fatigue between patients and controls

The comparison between the fatigue scores in the patients and the women in the control group shows greater fatigue in the control group, whether it is an average or median score (total fatigue score of 59.38 versus 51, 32 and median score 55.5 versus 52).

The highest average fatigue among patients was physical fatigue, followed by mental and general fatigue.

For the control group, the highest average concerned the drop in activity, followed by mental and general fatigue (Table 6).

Item	Average score of witnesses	Median score of witnesses	Average score of patients	Median score of patients
General fatigue	11,35	11,5	10,22	11
Physical fatigue	11,29	11	11,22	12,5
Decrease in activity	14,52	13,5	10,78	10
Decreased motivation	8,07	8	8,5	8
Psychic fatigue	14,15	12	10,6	11
Total score	59,38	55,5	51,32	52

Table 6: Comparison of fatigue scores.

Comparative study of fatigue between the patients and the control women without professional activity

The fatigue scores of the group of patients undergoing radiotherapy were compared with those of a subgroup of controls having no professional activity (Table 7).

Item	Average score of witnesses	Average score of witnesses without professional activity	Average score of patientes undergoing radiotherapy
General fatigue	11,35	9,68	10,22
Physical fatigue	11,29	10,03	11,22
Decrease in activity	14,52	10,06	10,78
Decreased motivation	8,07	7,06	8,5
Psychic fatigue	14,15	8,62	10,6
Score total	59,38	45,45	51,32

Table 7: Fatigue in patients and women controls not having a professional activity.

We found that the mean fatigue scores in the patients were higher than those in the subgroup of control women with no professional activity. In the latter as in the patients, fatigue predominates at the level of the dimensions of “decrease in activity” and “physical fatigue” and “general” while motivation is not affected.

Discussion

To our knowledge, our study is the only work evaluating the MFI 20 questionnaire in Arabic-speaking patients undergoing radiotherapy.

Our work constitutes one of the first pilot studies which assesses fatigue during radiotherapy for breast cancer in Tunisia [10]. Greenberg has shown through a series of 15 patients with localized breast cancer, that fatigue appears from the first week of irradiation and decreases during the second week then it increases in the third week and reaches a plateau and does not start to decrease only three weeks after the end of radiotherapy [11]. It is on this argument that our choice of study of the evaluation of fatigue at the third week of irradiation is based. Smets, *et al.* evaluated fatigue with MFI for a group of 250 patients followed for different types of cancers treated with curative intension. Among them 19% were followed for breast cancer. He showed increased fatigue during radiation therapy. Fatigue gradually decreases after [12-14].

Our study showed a high score of fatigue which predominates in its physical and psychic dimension while the motivation is not altered. This was also noted by Smets [8,9] (Table 8). The comparison between the fatigue scores in the patients and the women in the control group shows greater fatigue in our control group, whether it is a mean or median score.

The mean fatigue scores in the patients were higher than those in the subgroup of control women with no professional activity. In the latter as in the patients, fatigue predominates at the level of the dimensions of “reduced activity” and “physical fatigue” and “general” while motivation is not affected.

By comparing our results to those of the control groups of the Smets and Wafaa studies (using the MFI 20), we found that the average scores for the different dimensions of fatigue were significantly higher than those of the English and Arabic speaking control groups except for the decreased motivation for which the difference was minimal [3,9]. The mean of the different items of the MFI score varied between 8.23 and 9.9 for the controls of these 2 studies.

We also found a high percentage of patients who score more than the average of healthy subjects, this percentage varies between 56 and 73% for all items of the MFI except for the decrease in motivation (36%). Our results approximate those published by Smets as shown in table 8 [9].

Series	Our series of patients (n = 50)	Our group of witnesses	Our sub-group of witnesses without professional activity	Smets patients (n = 216) [9]	Smets Witnesses (n = 139) [9]	Wafaa Witnesses (n = 110) [3]
General fatigue	10.22	11,35	9,63	11.68	9.91	9.9
Physical Fatigue	11.22	11	10,03	11.71	8.79	9.4
Decrease in activity	10.78	13,25	10,06	11.69	8.69	8.9
Decreased motivation	8.5	8	7,06	8.73	8.23	8.4
Psychic Fatigue	10.6	12	8,68	7.55	8.33	9.4

Table 8: Average fatigue scores of our patients as well as those of Smets, Wafaa and control groups.

However, we cannot attribute the objectified fatigue in our patients to radiotherapy treatment since we have not evaluated it before this treatment and after all the more so since the fatigue is multifactorial (surgery, systemic treatments, social problems....) [4,5].

A search for studies published from 2000 to 2010 was carried out by TR de M Alcantara-Silva, *et al.* in the Pubmed, Scielo and Bireme databases, using the fatigue and radiotherapy descriptors and their correlations in Portuguese. They selected 12 articles (about breast cancer and gynecological cancers) from the 1085 found. The number of breast cancer studies was higher than for gynecological cancers [15]. The “Functional assessment cancer treatment subscale fatigue” (FACT F) assessment was the most used [15].

Eight publications were selected for fatigue during radiotherapy for breast cancer (Table 9) [15].

Authors	Fatigue assessment	Number	Average age (years)	Fatigue questionnaire
Geinitz., <i>et al.</i> 2001 [16]	Before radiotherapy 1 st week 2 months later	41	54	Hospital Anxiety and depression scale (HADS)
Geinitz., <i>et al.</i> 2004 [17]	Before radiotherapy 2 months later 2.5 years later	41	38	Visual Analogue scale for distress (VAS D)
Wratten., <i>et al.</i> 2004 [18]	Before radiotherapy While 2-6 weeks after	42	55.7	Functional assesement cancer treatment subscale G quality of life (FACT G)
Lavdaniti., <i>et al.</i> 2006 [19]	1 st -2 nd day of radiotherapy, 3 rd -4 th week and last week of radiotherapy	106	55	Piper Fatigue scale (PFS)
Moadel., <i>et al.</i> 2007 [20]	At the start of radiotherapy A month later 3 months later 6 months after start	128	54.8	Functional assesement cancer treatment subscale F: fatigue (FACT F)
Hwang., <i>et al.</i> 2008 [21]	At the start and end of radiotherapy	40	46.3	Brief Fatigue Inventory (BFI)
Lee., <i>et al.</i> 2008 [22]	Before and after radiotherapy then 7 months later	61	54	EORTC QL C30 supplement cancer you late
Montgomery., <i>et al.</i> 2009 [23]	Before and after radiotherapy then 7 months later	45	53.5	FACT F Visual Analogue Scale VAS

Table 9: Studies of fatigue linked to radiotherapy selected by TR de M Alcantara-Silva [15].

Geinitz., *et al.* found an increase in fatigue during radiotherapy for breast cancer and then a regression 2 months after the end of treatment [15-17]. The fatigue measured with the fatigue assessment questionnaire did not increase significantly during treatment, but the sub-scores on physical (p = 0.035) and cognitive (p = 0.015) fatigue were high during weeks 4 and 5 treatment. Emotional fatigue has not changed significantly.

In women with anxiety or depression the level of fatigue drops after radiotherapy compared to that before radiation but the fatigue persists for two and a half years after the end of treatment. In our study we evaluated fatigue during treatment for women without anxiety or depression [16].

Wratten., *et al.* have pointed out that fatigue becomes progressively worse during the first weeks of radiotherapy, reaching a plateau between the fourth week of treatment and the second week after the end of radiotherapy, returning to normal levels after six weeks from the end radiotherapy [18].

Lavdaniti, *et al.* considered that the fatigue levels of breast cancer patients undergoing radiotherapy were low in most cases and 1 in 8 patients presented with intense fatigue. Only the concept of vitality was significantly affected [19]. In our series 60% of patients had intense fatigue.

Patients included in the Moadel series had a fatigue score unchanged by radiotherapy [20], as were those in the Hwang study [21].

According to TR by M Alcantara-Silva, the variable number of subjects participating in the fatigue studies was very variable, which is a factor that can generate an inconsistency in the results [15-22]. In addition, the approach used to assess fatigue was different and complex. Indeed, this assessment was based on self-reported experiences, although specific questionnaires were used to measure fatigue [15-20]. The tests do not present any standardization of "measuring instruments", a fact attested by their varied content. The lack of standardization during the assessment may affect the reliability of the results. Therefore, it is not possible to say whether the levels of fatigue vary during treatment, along the plateau, and when they return to the first levels; due to methodological differences between the studies evaluated. Inconsistent findings limit the ability of studies to draw conclusions [15].

In most studies, the greatest interest of researchers is focused on the influence of fatigue on the quality of life of patients, while a few evaluate treatment strategies [15].

However, all researchers agree that the intensity and impact of fatigue in these patients differ negatively from those recorded for the general population, and therefore, this condition deserves special attention. Indeed it is widely known that fatigue is one of the most frequent and serious side effects of radiotherapy [15].

Besides fatigue, patients undergoing radiotherapy often have a poor quality of sleep which itself is a risk factor for fatigue [19-21].

In view of all this work, fatigue in women undergoing radiation for breast cancer is a real problem. Pharmacological interventions have rarely been described to reduce fatigue linked to cancer [15,24,25]. Several studies have shown encouraging results with non-pharmacological approaches such as physical exercise and psychological interventions [15,21,23-25]. Complementary and alternative medicine is gradually starting to take an interest in the management of symptoms linked to cancer [25,26]. A meta-analysis has shown the effectiveness of massages in reducing fatigue [26].

A randomized trial has shown that individual music therapy can reduce fatigue associated with radiation therapy in patients with breast cancer [27].

Conclusion

During radiotherapy for breast cancer patients have a high fatigue score which predominates in the physical and mental dimension while the motivation is not impaired. This should be taken into account when caring for and supporting patients with breast cancer. Paradoxically, the fatigue score of patients undergoing adjuvant radiotherapy for breast cancer is lower than that of the control group. This would be linked to the percentage of women with a professional activity among the witnesses. Indeed, the fatigue score of the patients is higher than that of the controls not having a professional activity, and this for all the dimensions of fatigue. To attribute patient fatigue to radiation, other studies are needed to assess fatigue before, during and after radiotherapy, possibly in different institutions with standardization of assessment methods.

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