Music Therapy Reduces Radiotherapy-Induced Fatigue in Patients With Breast or Gynecological Cancer: A Randomized Trial

Tereza Raquel Alcântara-Silva, MT, PhD[1] (ID),
Ruffo de Freitas-Junior, MD, PhD[1], Nilceana Maya Aires Freitas, MD, PhD[2],
Wanderley de Paula Junior, MS[3], Delson José da Silva, MD, PhD[1,4],
Graziela Dias Pinheiro Machado, RN[3], Mayara Kelly Alves Ribeiro, MT, MS[5],
Jonathas Paiva Carneiro, MT[6], and Leonardo Ribeiro Soares, MD[1]

Abstract

Purpose: To investigate the influence of music therapy on the reduction of fatigue in women with breast or gynecological malignant neoplasia during radiotherapy, since it is one of the most frequent side effects of this type of treatment, and may interfere with self-esteem, social activities, and quality of life. **Experimental Design:** Randomized controlled trial (control group [CG] and music therapy group [MTG]) to assess fatigue, quality of life, and symptoms of depression in women undergoing radiotherapy using the Functional Assessment of Cancer Therapy: Fatigue (FACT-F) version 4, Functional Assessment of Cancer Therapy–General (FACT-G) version 4, and Beck Depression Inventory in 3 separate times, namely, during the first week of radiotherapy, on the week of the intermediary phase, and during the last week of radiotherapy. Individual 30- to 40-minute sessions of music therapy with the presence of a trained music therapist were offered to participants. **Results:** In this study, 164 women were randomized and 116 (63 CG and 53 MTG) were included in the analyses, with mean age of 52.90 years (CG) and 51.85 years (MTG). Participants in the MTG had an average of 10 music therapy sessions, totaling 509 sessions throughout the study. FACT-F results were significant regarding Trial Outcome Index ($P = .011$), FACT-G ($P = .005$), and FACT-F ($P = .001$) for the MTG compared with the CG. **Conclusions:** Individual music therapy sessions may be effective to reduce fatigue related to cancer and symptoms of depression, as well as to improve quality of life for women with breast or gynecological cancer undergoing radiotherapy. Further well-designed research studies are needed to adequately determine the effects of music therapy on fatigue.

Introduction

Fatigue is one of the most commonly experienced cancer symptoms, affecting 70% to 100% of the people undergoing cancer treatments.[1,2] Cancer-related fatigue (CRF) is defined by the European Association for Palliative Care as a subjective symptom of tiredness, weakness, or lack of energy.[3] The National Comprehensive Cancer Network describes CRF as a subjective, distressing, and persistent symptom of physical, emotional, and/or cognitive tiredness or exhaustion related to the disease or its treatment.[4]

In 2012, 41% of all new female patients of neoplasia worldwide had breast or gynecological cancer.[5] A review study demonstrated that fatigue is a frequent symptom in patients undergoing radiotherapy and may become a factor that limits or even prevents the continuity of treatment.[2]

[1]Federal University of Goias (UFG), Goiânia, GO, Brazil
[2]Centro Brasileiro de Radioterapia, Oncologia e Mastologia (CEBROM), Goiânia, GO, Brazil
[3]Instituto Integrado de Neurociências (IINEURO), Goiânia, GO, Brazil
[4]Araújo Jorge Hospital, Associação de Combate ao Câncer em Goiás (ACCG), Goiânia, GO, Brazil
[5]Associação de Pais e Amigos dos Excepcionais (APAE), Goiânia, GO, Brazil
[6]Federal University of Rio de Janeiro (UFRJ), Brazil

Corresponding Author:
Tereza Raquel Alcântara-Silva, Universidade Federal de Goiás, Campus II, Samambaia, Avenida Esperança, s/n, Campus Universitário, 74690-900 Goiânia, GO, Brazil.
Email: terezaraquel.mas@gmail.com

Fatigue treatment may include pharmacological and nonpharmacological interventions. However, interventions for CRF have been largely unsuccessful.[6] The use of music for therapeutic purposes is indicated in cancer treatment for anxiety and depression, and for also for fatigue, based on clinical trials.[7,8] A professional music therapist adjusts the experiences that music can offer to the patients' needs in a therapeutic relationship.[9] A reduction of anxiety and depression in cancer patients who received music therapy was observed in some studies.[7,10] However, in the case of fatigue, one recent review indicates that the trials on fatigue offer only low-quality evidence, since they are poorly designed.[7] Therefore, this study aimed to verify the influence of music therapy on fatigue in patients with breast and gynecological cancer undergoing radiotherapy.

Method

Study Design

This was a prospective, randomized study using music therapy to alleviate fatigue and depressive symptoms.

Participants

Participants were female patients recruited from a cancer treatment hospital located in the Midwest region of Brazil. Inclusion criteria were the following: (1) diagnosis of breast or gynecological cancer, (2) age between 20 and 80 years, (3) scheduled to receive radiotherapy (teletherapy or brachytherapy) planned for 20 or more sessions, and (4) score of 70 or more points in the Karnofsky Performance Scale Index. Exclusion criteria were the following: (1) already undergoing radiotherapy, (2) hemoglobin levels equal or less than 10 mg/dL, (3) undergoing psychotherapeutic treatment during the study period, (4) using antidepressants during the study period, and (5) diagnosis of other types of cancer. Furthermore, the patients who did not attend at least 75% of music therapy sessions or had to interrupt radiotherapy for more than 10 days were discontinued.

Procedures

To carry out the randomization, 164 sealed envelopes containing the names of the groups (control group [CG] and music therapy group [MTG]) in identical proportions were used (Figure 1). The participants were evaluated regarding fatigue and quality of life at 3 different times: (1) at the initial phase, during the first week of radiotherapy; (2) at the intermediary phase, during the third or fourth weeks of radiotherapy; and (3) at the final phase, during the last week of radiotherapy. The symptoms of depression were assessed at the initial and final phases of the study. The questionnaires were completed in the same period, independently of

the group. The CG received radiotherapy in the same hospital as the MTG.

Instruments

The sociodemographic variables were collected using a questionnaire developed specifically for this study. To assess fatigue, the Functional Assessment of Cancer Therapy Fatigue (FACT-F) version 4[11] was applied in its validated Portuguese version.[12] The FACT-F scores range from 0 (intense fatigue) to 52 (no fatigue).[13] To measure the intensity of depression, the Beck Depression Inventory was employed in the validated Portuguese version.[14,15] This is a self-report composed of 21 items, with a 4-point scale for each item ranging from 0 to 3, and the total score is the sum of all items, ranging from 0 (no depression) to 63 (most severe depression).[14,15] At all scales, the participants responded to how they felt over the past week.
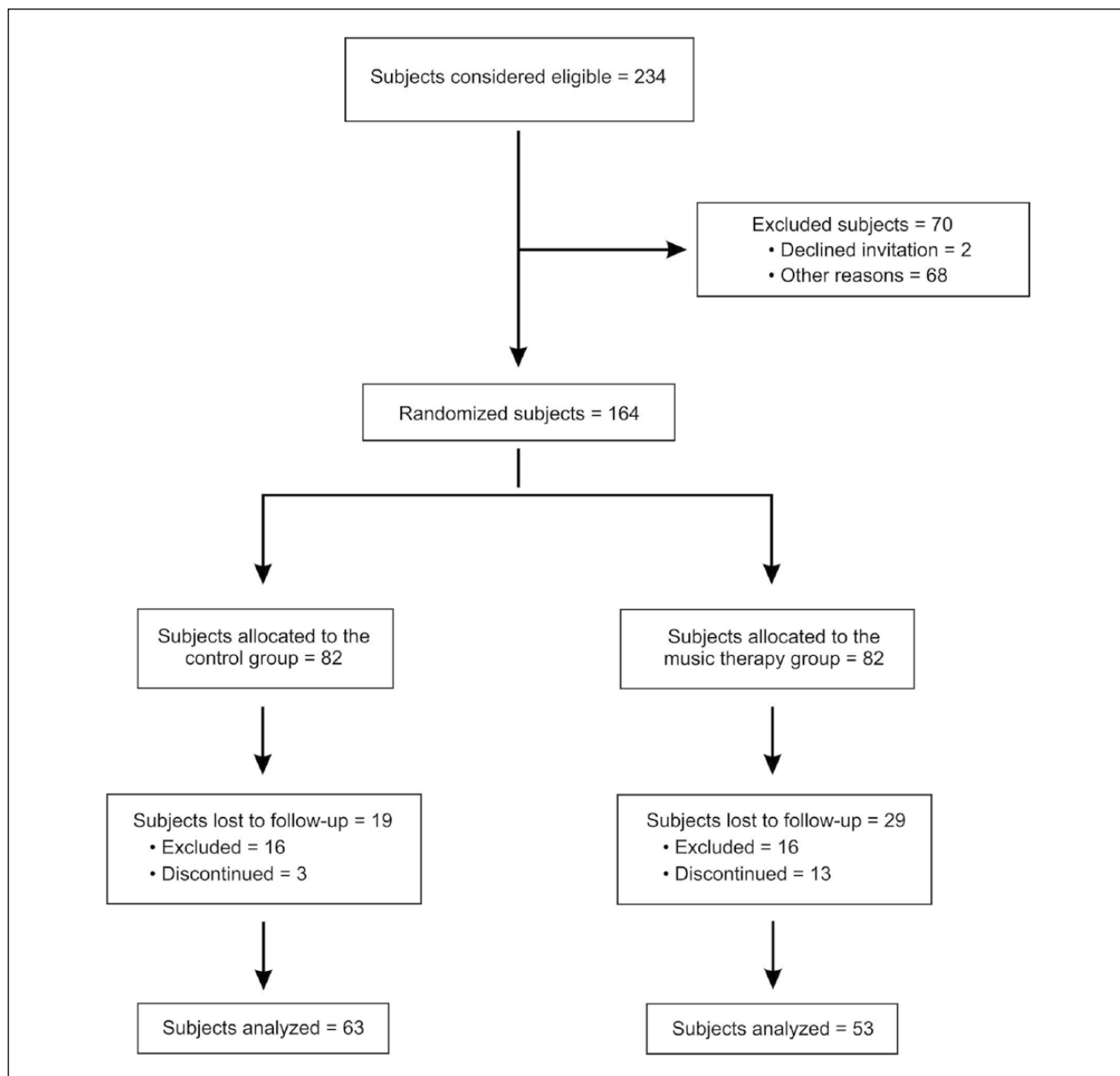
Music Therapy

The music therapy sessions were conducted by a trained and experienced music therapist (TRM Alcântara-Silva). The participants in the MTG had individual 30- to 40-minute music therapy sessions twice a week right before the radiotherapy sessions, in the therapist's office, in a cancer treatment hospital.

The strategy chosen was a therapeutic period listening to music at 3 different times of each session, following the protocol established for this research, that is, first listening, second listening, and third listening. The selection of songs for the first and third listening of each session was performed by the music therapist based on her own repertoire of the baroque, classical, and romantic periods.

For the first listening, 12 songs were chosen, which were instrumental, with a slow tempo, a tone, and regular pulse. These features generate a consonant melody, leading to more pleasure during listening because of the activation of the cortical region of the brain, related to pleasurable responses to consonant musical stimuli.[16] The music therapist previously determined the sequence of the songs, so that all the patients would listen to the same song in the first music therapy session, in the second one, and so forth. Since the total number of sessions ranged from 8 to 12, the last song in the list was played in the last session of each patient, regardless of the number of the session.

The selection of songs for the second listening was patient-chosen by participants in the MTG, each of whom gave the music therapist a list of her favorite songs. The selection of the songs for the third listening followed the same pattern already described for the first one, except that the tempo was faster, and the last song in the period, also chosen to be played in the last session of each patient, regardless of the number of the sessions, was played by an orchestra and singer.

Figure 1. Diagram of randomization.

The equipment used in the music therapy sessions included the following: a fourth-generation iPod Nano (Apple Inc, Cupertino, CA) and a Powerpack model SK-2 speaker. The music therapy sessions were conducted according to a specific protocol developed for this study and consisted of the following: (1) welcoming the patient (5 minutes), a moment dedicated to receive the patient and collect the study variables; (2) first listening (5 minutes); (3) second listening (5 minutes); (4) talking (5 to 15 minutes), a period of time for the patients to the freely express their feelings; (5) third listening (5 minutes); and (6) ending the session (5 minutes), a moment dedicated for brief personal reflection and patient leaving.

Statistical Analysis

Data were analyzed using dispersion and central tendency measurements. Sociodemographic results and Beck Depression Inventory variables were analyzed using the χ^2 test with analysis of relative risk. For FACT-F variables, the Wilcoxon test and the Kruskal-Wallis test were applied to assess the intragroup and intergroup statistical differences

Table 1. Sociodemographic Characteristics of the Participants According to the Group of Inclusion in the Study.

	CG		MTG			
Variables	n	%	n	%	P	95% CI
Race						
Caucasian	20	34.5	22	44.9		1.00
African	6	10.3	3	6.1	.25	0.45 (0.10-2.06)
Asian	6	10.3	2	4.1	.15	0.30 (0.05-1.67)
Indian	1	1.7	0	0.0	.30	0.47 (0.34-0.65)
Mulatto	25	43.1	22	44.9	.60	0.80 (0.34-1.84)
Marital status						
Married	38	64.4	36	69.2		1.00
Single	10	16.9	6	11.5	.41	0.63 (0.21-1.92)
Widow	5	8.5	5	9.6	.93	1.056 (0.28-3.95)
Separated	2	3.4	1	1.9	.60	0.52 (0.04-6.07)
Divorced	4	6.8	4	7.7	.94	1.05 (0.24-4.54)
Education level						
Illiterate	5	9.8	5	10.9		1.00
Elementary school level 1	16	31.4	13	28.3	.77	0.81 (0.19-3.42)
Elementary school level 2	14	27.5	9	19.6	.56	0.64 (0.14-2.87)
High school	10	19.6	11	23.9	.90	1.10 (0.24-4.96)
College	6	11.8	8	17.4	.72	1.33 (0.26-6.80)
Physical activity						
Sedentary	42	82.4	39	88.6	.33	1.00
Active	9	17.6	5	11.4	.44	1.34 (0.64-2.82)
Tobacco consumption						
No	34	65.4	36	73.5		1.00
Yes	4	7.7	5	10.2	.81	1.18 (0.29-4.76)
Ex-smoker	14	26.9	8	16.3	.21	0.54 (0.20-1.45)
Alcohol consumption						
No	52	100.0	48	98.0		1.00
Yes	0	0.0	1	2.0	.30	—

Abbreviations: CG, control group; MTG, music therapy group; CI, confidence interval.

between the CG and the MTG, respectively. The results were considered statistically significant at the 95% confidence interval when $P < .05$.

Ethics Statement

This study was approved by the Research Ethics Committee of the Associação de Combate ao Câncer em Goiás (CEP/ACCG, No. 054/09) and it was conducted in accordance with the ruling principles of the Helsinki Convention. The participants were volunteers, and they signed a free and informed consent statement before their inclusion in the study, having received information about the study, its aims, and its probable side effects and future advantages.

Results

The sociodemographic characteristics of the 116 participants are presented in Table 1. The mean age of the participants was 52.90 (±10.26) years for the CG and 51.85

(±10.60) years for the MTG. The clinical characteristics of the participants are shown in Table 2. The main reasons for exclusion of the patients were the use of antidepressants during the study (n = 3), the hemoglobin level below 10 mg/dL (n = 2), and delayed onset of radiotherapy (n = 2). The main reasons for discontinuation were interruption of radiotherapy for more than 10 days (n = 7), number of music therapy sessions less than 75% of the planned sessions (n = 5), and temporal impossibility to participate in the sessions (n = 3) or to respond to the questionnaire (n = 6), in addition to 5 patients who left the study without justification.

Participants in the MTG (n = 53) had an average of 10 music therapy sessions, totaling 509 individual appointments during the study. For these patients, all the FACT-F variables were statistically significant ($P < .05$): Trial Outcome Index (TOI), Functional Assessment of Cancer Therapy: General (FACT-G), and FACT-F (Table 3 and Figures 2-4).

Comparing the variables of the 3 phases of assessment within the same group (Wilcoxon test), the data obtained for

Table 2. Clinical Characteristics of the Participants and Type of Treatment According to the Group of Inclusion in the Study.

	CG		MTG			
Variables	n	%	n	%	P	95% CI
Types of cancer						
Breast	47	73.4	43	81.1		1.00
Gynecological	17	26.6	10	18.9	.32	0.64 (0.26-1.55)
Staging						
In situ	4	6.5	0	0.0		1.00
I	19	30.6	10	18.9	.16	1.52 (1.17-1.98)
II	16	25.8	20	37.7	.03	2.25 (1.56-3.24)
III	19	30.6	16	30.2	.08	1.84 (1.36-2.50)
IV	4	6.5	6	11.3	.04	2.50 (1.17-5.34)
Surgery						
No	9	14.3	9	17		1.00
Yes	54	85.7	44	83	.69	0.81 (0.30-2.23)
Chemotherapy						
No	22	34.9	14	26.4		1.00
Yes	41	65.1	39	73.6	.32	1.50 (0.67-3.33)
Radiotherapy (no. of sessions)						
21-25	20	31.7	15	28.3		1.00
26-30	43	68.3	37	69.8	.73	1.14 (0.51-2.55)

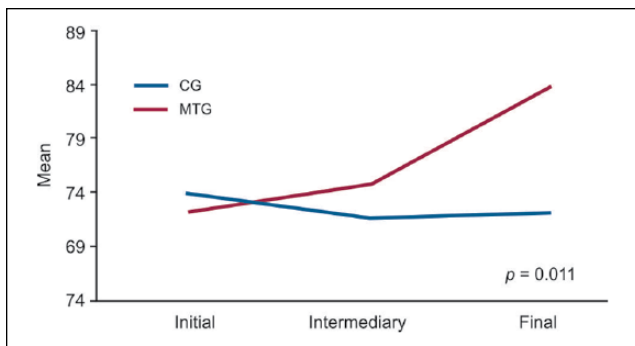Abbreviations: CG, control group; MTG, music therapy group; CI, confidence interval.

Table 3. Assessment of Fatigue in the 3 Domains of the FACT-F During Radiotherapy According to the Group of Inclusion in the Study.

Variables	Timing of Assessment	Group	n	Mean Values	P
TOI	Initial	CG	65	61.15	.561
		MTG	53	57.47	
	Intermediary	CG	54	49.64	.617
		MTG	47	52.56	
	Final	CG	64	51.74	.011
		MTG	53	67.76	
FACT-G	Initial	CG	65	58.20	.647
		MTG	53	61.09	
	Intermediary	CG	54	47.23	.166
		MTG	47	55.33	
	Final	CG	64	50.93	.005
		MTG	53	68.75	
FACT-F	Initial	CG	65	59.28	.940
		MTG	53	59.76	
	Intermediary	CG	54	48.34	.328
		MTG	47	54.05	
	Final	CG	64	51.59	.009
		MTG	53	67.95	

Abbreviations: FACT-F, Functional Assessment of Cancer Therapy: Fatigue; TOI, Trial Outcome Index; CG, control group; MTG, music therapy group; FACT-G, Functional Assessment of Cancer Therapy: General.

the CG with FACT-F did not present significant response in the domains TOI, FACT-G, and FACT-F, whereas the data obtained for the MTG showed significant improvement in the same domains ($P < .01$). Patients in the MTG showed improvement in symptoms of depression, which were reduced to the minimum level ($P = .005$), and a 74% reduction in risk of depression (relative risk = 0.26%; 95% CI = 0.10-0.70).
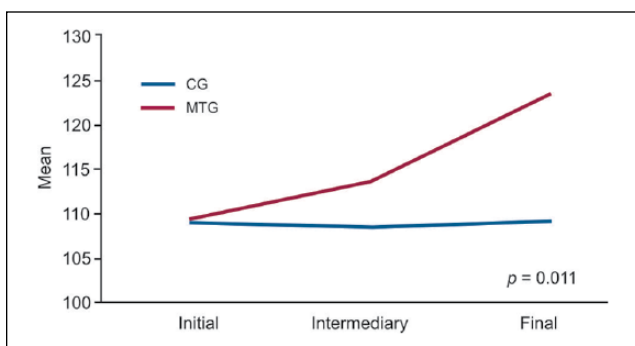
Figure 2. Assessment of the domain Trial Outcome Index during radiotherapy, according to the group of inclusion in the study, using the Functional Assessment of Cancer Therapy: Fatigue.
Abbreviations: CG, control group; MTG, music therapy group.
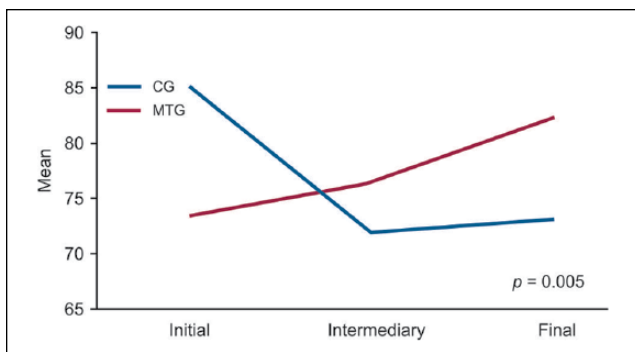
Figure 3. Assessment of the variable quality of life during radiotherapy, according to the group of inclusion in the study, using the Functional Assessment of Cancer Therapy: Fatigue.
Abbreviations: CG, control group; MTG, music therapy group.

Figure 4. Assessment of the variable fatigue during radiotherapy, according to the group of inclusion in the study, using the Functional Assessment of Cancer Therapy: Fatigue.
Abbreviations: CG, control group; MTG, music therapy group.

Discussion

The present study indicated a possible association between fatigue and quality of life, since the participants in the MTG

Table 4. Comparative Analysis of Categories (χ^2 test) During Radiotherapy According to the BDI.

| Variables | CG | | MTG | | | |
	n	%	n	%	P	RR (95% CI)
BDI—Initial phase						
Minimum	36	65	34	64	.88	1.00
Mild to intense	9	16	10	19		0.97 (0.65-1.44)
BDI—Final phase						
Minimum	35	64	46	87	.005	1.00
Mild to intense	11	20	5	9		0.26 (0.10-0.70)

Abbreviations: BDI, Beck Depression Inventory; CG, control group; MTG, music therapy group; RR, relative risk; CI, confidence interval.

experienced improvements in both aspects after the music therapy sessions. This finding is corroborated by a recent meta-analysis that pointed to a decrease in fatigue and an increase in quality of life of cancer patients after music interventions.[7]

In a comparative analysis of the CG and MTG, taking into consideration the 3 phases of assessment, the fatigue profile was at similar levels at the beginning of the study for patients in both groups and improved in the final phase of treatment in both groups. However, the participants in the MTG showed statistically significant improvement compared with the CG patients under the same conditions (Figures 2-4). Therefore, it is possible to infer that the participants in the MTG experienced improvement in fatigue symptoms because of music therapy.

In this study, music therapy significantly reduced the symptoms of depression, and hence it can be considered an adjuvant therapy for the treatment of cancer patients (Table 4). This outcome is in accordance with other results described in the literature.[17-19] The emotional support provided by music therapy may justify the statistically significant improvement of fatigue symptoms experienced by the participants in the MTG. From the neurophysiological point of view, the music-evoked emotions can modulate activity in virtually all limbic and paralimbic brain structures. These structures are crucially involved in the initiation, generation, detection, maintenance, regulation, and termination of emotions, which are constantly present in the life of the individual. Therefore, at least some music-evoked emotions involve the very core of adaptive neuro-affective mechanisms.[20,21] Thus, music therapy can bring several benefits to cancer patients, helping them to find ways to deal with stress, fear, and loneliness.[22,23]

Nonetheless, the benefits of music therapy in the management of fatigue remain uncertain and some authors reported no positive effects in improving physical and psychological aspects of cancer patients.[7,24] This difference may be explained by differences in methods of music therapy intervention, or even in the techniques applied and

the number of sessions offered.[25] Therefore, our randomized trial is a contribution to this literature because it studies music therapy in the radiotherapy setting for Brazilian patients.

In this study, most songs chosen by the patients approached themes similar to the feelings they were experiencing during radiotherapy, such as loss, loneliness, and sorrow. Familiar songs play an important role in music therapy, because they allow latent contents to emerge, and they also help the patients to become aware of their problems and look for more adaptive coping strategies, leading to a better understanding of the treatment, and alleviation of the symptoms for most individuals.[20]

The biological facts underlying the results found in this study may be connected to the relationship of music with deep brain structures involved in the processing of emotions.[17,18] Therefore, music plays a major role in self-regulation of emotional contexts.[26] Music is also involved in the regulation and genetic expression of dopamine,[27] as well as in the alterations in the levels of serotonin, cortisol, and oxytocin.[28] Hence, it is possible to affirm that the positive response obtained with the action of music in the therapeutic context, applied by a qualified music therapist, is based on biopsychosocial grounds.

Fatigue is still underdiagnosed, although it is one of the most important symptoms affecting cancer patients. Because of the indisposition it causes, in many cases fatigue may limit or even prevent the continuity of radiotherapy. Therefore, fatigue treatment should be given a high priority in a multidisciplinary approach of pharmacotherapeutic and nonpharmacotherapeutic interventions. However, it is highly important to diagnose it during the initial appointments, so that it can be properly treated, inasmuch as fatigue level before the treatment is a significant predictor of this condition during and after radiotherapy.[29] Moreover, it is necessary to enlighten patients and family members about fatigue symptoms and treatment. Interdisciplinary teams are valuable to adequate patients' individual needs.

In the present study, the discontinuation rate was higher than expected. Some of the losses to follow-up may be attributed to the schedule of the appointments, radiotherapy and chemotherapy side effects, and family situations.

Among the limitations of the study, the difficulty of blinding the participants (open-label study) and the small individual variations in the music therapy sessions are worth mentioning. Therefore, the interpretation of the study results should be cautious, because of the nonblinded nature of the study. Nonetheless, these features are inherent to studies involving musical interventions. Another limitation was the absence of a time-and-attention control group, considering the possibility of a placebo effect because of the time spent with a therapist and the personal attention received from the therapist.

Finally, the following suggestions are aimed at contributing to future studies: (1) create programs to inform patients and family members about fatigue and its repercussion in breast or gynecological cancer patients' quality of life and treatment; (2) implement educational programs to enlighten patients and family members about fatigue symptoms; (3) establish a protocol for the evaluation of CRF, as well as for screening and treating it before and during radiotherapy; and (4) add a music therapist to the multiprofessional team in charge of the treatment of fatigue and other symptoms experienced by patients during radiotherapy.

Conclusion

Music therapy can be applied as an integrative treatment during radiation therapy and has the potential to affect fatigue. In this study, statistically relevant responses were found regarding fatigue, quality of life, and symptoms of depression. Continuous assessment of results, in the beginning, during, and after radiotherapy is also relevant. Moreover, assessment during radiotherapy allows professionals to rethink and adjust the procedures aimed to achieve effective responses to treatment, as well as minimize the number of patients who abandon it. Further well-designed research studies are needed to adequately determine the effects of music therapy on fatigue.

ORCID iD

Tereza Raquel de Melo Alcântara-Silva (iD) https://orcid.org/0000-0002-9363-5747

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