

Effect of Music Therapy Combined With Aerobic Exercise on Sleep Quality Among Patients With Chemotherapy After Radical Mastectomy: Results From a Randomized Controlled Trial

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Abstract

Background: The morbidity and mortality of breast cancer have gradually increased in recent years, seriously threatening women's health. Sleep disorder is one of the most common symptoms in patients with breast cancer. In recent years, with the increasing awareness of the importance of the quality of life of cancer patients, reducing symptoms and improving the quality of sleep have become the focus of cancer research. Some studies shown that music therapy can effectively promote the sleep quality. Other studies have indicated that aerobic exercise has the positive effect on sleep quality. However, the effects of these interventions on sleep quality of breast cancer patients, especially those in the chemotherapy after radical mastectomy is still unclear.

Objective: The aim of this study was to explore the effect of music therapy combined with aerobic exercise on the sleep quality of patients undergoing chemotherapy after radical mastectomy.

Methods: A randomized controlled trial was conducted at Breast Disease Diagnosis and Treatment Center, Shaanxi Province Tumor Hospital from November 2017 to January 2019.

A total of 100 female breast cancer patients who underwent modified radical mastectomy (MRM) or extensive radical mastectomy (ERM), were recruited through convenient sampling, and randomly allocated into an intervention group of 51 patients and a control group with 49 patients respectively. The intervention group accepted music therapy combined with aerobic exercise from the first to the sixth admission to hospital for chemotherapy in addition to the routine nursing care, while the control group received only routine nursing care. Sleep quality of these patients were measured 3 times, eg, at the end of 10 days, the first cycle of chemotherapy, the third cycle of chemotherapy and the end of the sixth cycle of chemotherapy using Pittsburgh sleep quality index (PSQI), and to compare the total score of sleep quality and the difference of each factor between the two groups. A linear mixed model was used to measure the effect on PSQI of patients after controlling for other confounding factors.

Results: The mean score of sleep quality of breast cancer patients who received chemotherapy after radical mastectomy, were 8.86 ± 2.34 .

The patients with PSQI score greater than 7 points accounted for approximately 89.0%. Moreover, there were more than half of the patients with scores of subjective sleep quality, sleep duration, sleep disturbance and daytime dysfunction higher than 2 points. 56.0% of patients had the problem of poor subjective sleep quality; 42.0% of patients had the trouble in falling asleep; 34.0% of patients had sleep disturbance (easy to get up, get up early, frequently to go toilet at night). About 34.0% of patients slept less than 6 hours, and had daytime dysfunction such as energy shortage and fatigue.

Significant improvements from baseline in all indices for sleep quality measurement were observed throughout the intervention period from 1st post-test to 3rd post-test.

With the increase of chemotherapy cycle, the total score of PSQI and the score of sleep quality in the intervention group showed a decreasing trend. However, change in PSQI-total had increased from 1st post-test to 3rd post-test gradually increased in the intervention group (difference between groups: $-1.31(-2.05,-0.57)$ to $-2.102(-2.84,-1.36)$). On the contrary, significant increases in changes of the PSQI-total in control groups from 1st post-test to 3rd post-test was clear (difference between groups: $0.55(-0.18,1.2752)$ to $2.75(2.02,3.47)$).

Limitations: The data were self-reported, which could be influenced by many potential factors, and no biomarkers or physiological measurements were done, which need to be further explored. What's more, bigger sample size was needed in the future studies to enhance the representativeness of the subjects.

Conclusions: Music therapy combined with aerobic exercise intervention can significantly improve the sleep quality of female breast cancer patients with chemotherapy after radical mastectomy, and it has a good continuous improvement effect on many aspects of reactive sleep.

Introduction

Breast cancer (BC) is the most commonly diagnosed cancer in the vast majority (83%) of countries and the leading cause of cancer deaths in more than 100 countries [1]. According to the Global Cancer Statistics Report 2018: estimates of the incidence and mortality of 36 cancers in 185 countries [2], there were approximately 2.1 million new cases of breast cancer worldwide in 2018, accounting for nearly a quarter of female cancer cases, with the standardized incidence and mortality rates of 46.3 per 100,000 and 13.0 per 100,000, respectively. The data of China National Cancer Center show that the number of new cases of breast cancer in China is 30.4 million in 2015, and the number of deaths is 70,000, which is the first-time malignant tumor of Chinese women. Compared with other malignant tumors, breast cancer has the highest cure rate. With the improvement of diagnosis and treatment technology of breast cancer and the wide application of effective comprehensive treatment methods, the survival time of breast cancer patients has been prolonged [3]. The five-year survival rate of breast cancer can reach 85.9% and the 10-year survival rate can reach 80.0% [4]. Surgery combined with chemotherapy has become an important method for the treatment of breast cancer. Treatment can easily lead to adverse reactions to chemotherapy, physiological and psychological dysfunction and so on, which has a serious impact on the sleep quality of patients [5].

Sleep disorder is one of the most common symptoms in patients with breast cancer. Sleep is the key biological behavior to maintain the best immunity, endocrine function and cell metabolism, and also plays an important role in hormone level, emotion and cognitive behavior [6–7]. Domestic studies have shown that the incidence of sleep disorders in patients with breast cancer is as high as 90% or more [8]. Sleep disorder usually interacts with anxiety, depression, cancer fatigue, pain and other symptoms, which not only reduces the quality of life of patients with breast cancer, but also is a risk factor for the progress, metastasis and prognosis of breast cancer [6, 9]. In recent years, with the increasing awareness of the importance of the quality of life of cancer patients, reducing symptoms and improving the quality of sleep have become the focus of cancer research.

It is shown that music therapy can relieve mild and moderate pain, and can effectively relieve the poor sleep quality caused by negative emotions such as depression and fear in cancer patients [10–11]. The music therapy can also interfere with the release of the substance such as morphine and the like, relieve the anxiety and depression mood of the patient, and further play a sedative and hypnotic effect [12]. Other studies have shown that aerobic exercise can improve neuroendocrine function and increase the levels of serotonin and endorphin [13–14], which can relieve fatigue, enhance body function, improve cardiopulmonary function and improve psychological and mental state, which is of positive significance for improving sleep quality [15–16].

Despite the advantage of music therapy combined with aerobic exercise mentioned above, the effects on sleep quality of breast cancer patients, especially among breast cancer patients in the chemotherapy after radical mastectomy is still not known. Therefore, we conducted this randomized controlled trial to explore the effect of music therapy combined with aerobic exercise on sleep quality of breast cancer patients after radical mastectomy. We also attempt to further seek for effective nursing methods to improve and enhance sleep quality of the patients.

Materials And Methods

All Methods of this study were performed in accordance with the relevant guidelines and regulations.

Study design and participants

This study utilized clinical trial with two arms, no blind, which was conducted at Breast Disease Diagnosis and Treatment Center, Shaanxi Provincial Tumor Hospital from July 2017 to June 2019.

The target population was female breast cancer patients who received chemotherapy about 10-15 days after modified radical mastectomy (MRM) or extensive radical mastectomy (ERM). Chemotherapy options include TEC, dense AC sequential dense Paclitaxel or Docetaxel, AC, TC, etc., that is, Paclitaxel or Docetaxel, Epirubicin or Adriamycin and Cyclophosphamide.

Personal controlled dose of these drugs were calculated based on patients' weight and body surface area (BSA). The subjects received a total of 6-8 complete courses of treatments, which took 8 days with 21 days intervals in every complete course.

The sample size was determined by the levels of questionnaire dimensions. The calculation equation of sample size was presented on follows: $\text{Sample size} = [\text{Max}(\text{dimensions}) \times (10-20)] \times (1+15\%)$

With Pittsburgh Sleep Quality Index table contains 7 dimensions, the minimum number of sample size of our study was approximately 80. Considering the situation of nonresponse, however, we expanded the sample size by 30% to 40%. The patients were recruited in this study by the convenient sampling method if they meet the following inclusion criteria: (1) they were willing to join the study voluntarily; (2) they must have normal cognitive state and ability to express clearly; (3) no physical disability; (4) they were clearly diagnosed with breast cancer of TNM staging based on fast pathology slide and paraffin section. Patients with consciousness disorders, mental or neurological disorders, mental, hearing or cognitive impairments, physical disabilities, and breast cancer with other cancers will be excluded. Stage IV breast cancer patients were also excluded. By the end, we expected to recruit 110 subjects. The patients were randomly allocated to two groups using a randomized code generally by computer software with 55 in each group.

Intervention Procedures

The protocol was reviewed and approved by the Human Research Ethics Committee of Shaanxi Provincial Tumor Hospital. This study was registered in the Chinese Clinical Trial Registry (ChiCTR2100042975, 03/02/2021). Questionnaire survey method is adopted. The questionnaire is interpreted with unified guidance language, distributed and recovered on site. Based on identification numbers in hospital, all the patients are randomly allocated into the experimental and control group by random number table method. Before the study, all patients were given all related information about the study and signed "informed consent form". All patients were numbered according to the case number, Patients in the control group were cared with routine perioperative nursing and chemotherapy nursing. The intervention group accepted music therapy combined with aerobic exercise from the first admission to hospital for chemotherapy to the sixth admission to hospital for chemotherapy in addition to the routine nursing care, and implemented 30 min every time and 2 times every day. Patients were visited regularly during intervention by researchers, and supervised to adhere to music therapy combined with aerobic exercise procedures. During the intermittent period of chemotherapy treatment, moreover, patients in the intervention group were followed-up by telephone and encouraged to stick to intervention procedures. Control group patients received the same perioperative nursing care and chemotherapy, except for music therapy combined with aerobic exercise intervention.

Music therapy combined with aerobic exercise

First of all, patients gathered at the patient service center in a quiet and comfortable environment to relax their mind and body. They can also choose music according to their own preference and wear headphones after treatment. They can

listen repeatedly with the volume of 30dB ~ 50dB. Music media library includes Chinese classical folk music, world famous music, music therapy association (AAMT) recommended nature music series CD and relaxing music, a total of 334 pieces of music, all instrumental music. Because of the interference effect of the lyrics, songs and operas are not included. Specific tracks such as "Yao nationality dance", "Two springs reflect the moon", "Blue Danube river", "Spring", "Clouds chasing the moon", "Destiny symphony", etc. After the establishment of music library, it was copied into MP5 for use by patients in the intervention group twice a day for 30min each time until the end of the 6th cycle of chemotherapy [17].

Along with music therapy, in the meanwhile, aerobic exercise was also carried out in the intervention. Aerobic exercise for 15 ~ 20 min before the upper extremity joints and the whole body of each joint exercises, on the basis of aerobic exercise, including head, head rotation, single shoulders, shoulders, arm forward, lift on lateral flexion, left and right sides of, lift on forward bends, pendulum is before and after hip, hip, or jump around step, step swing arm, a total of 12 knots. Repeat the whole set of movements for 2-3 times, and the effective exercise time is 20 ~ 25 minutes. Finishing activities were performed for another 10 minutes, including treading in place, upper limb swing and relaxation, etc [18]. The effective exercise intensity of the whole scheme was controlled within the range of the target rate of the patients, with target heart rate = (220-age-quiet heart rate) × (45% ~ 60%) + quiet heart rate.

Aerobic exercise requires the patients to have group training every Monday, Wednesday and Friday afternoon, lasting until the end of the 6th cycle of chemotherapy. Those who cannot exercise at the specified time due to special reasons should participate in weekly supplementary training. Intervention team members visited patients regularly during the hospital stay, helped patients adhere to the intervention, and conducted regular telephone follow-up during the treatment interval to encourage patients to continue the intervention.

Measurement of sleep quality

In this study, the social and demographic data and disease-related conditions of the patients were collected by general questionnaire, and the Sleep Quality of the patients was evaluated by Pittsburgh Sleep Quality Index (PSQI). The questionnaire of general situation was designed by the Breast Disease Diagnosis and Treatment Center of Shaanxi Province Tumor Hospital and completed under the guidance of relevant experts. It included demographic data and disease related conditions. PSQI was designed by Pittsburgh psychiatrist Buysse organically, which could evaluate sleep quality and sleep quantity simultaneously within one month.

19 self-rated and five peer-rated items are included in the PSQI, of which the 19th self-rated item and all five peer-rated items are not used for score. The rest of the 18 self-rated items are divided into seven dimensions, including subjective sleep quality, fall-asleep time, sleep duration, sleep efficiency, sleep disturbance, use of sleep medication, daytime function, each of which are weighted 0-3 scores. Based on the sum of the seven components with a range of 0-21, when the total score of PSQI is much higher, sleep quality is much worse. The PSQI should be completed in 5-10 minutes [19]. In 1996, Liu Xianchen et al had translated the scale into Chinese, and also evaluated the reliability and validity. It was found a good internal consistency and reliability using the scale, which is suitable for Chinese patients. In the study, Pittsburgh sleep quality index greater than 7 was used as boundary value of sleep quality problem among adults in China [20]. Pittsburgh sleep quality index (PSQI) was used to evaluate the sleep quality of patients in the two groups at the end of 10 days, the first cycle of chemotherapy, the third cycle of chemotherapy and the sixth cycle of chemotherapy, respectively.

Quality control

In the study, random controlled trial study was applied. Before the study, a group was established to implements music therapy combined with aerobic exercise intervention, and all research staff was trained uniformly according to the

detailed standard guidelines and training protocols developed in the pilot study. After the train, only the eligible research staff who passed the theory and practice examination, would be required to conduct this research. During the research, Subjects were also re-interviewed when errors and/or missing values were detected. For those absent patients within the prescribed time due to special reasons, they had to take part in additional training every week.

Statistical analysis

In the follow-up treatment, 4 patients in the intervention group were lost to follow-up, and 6 patients in the control group. Finally, 51 patients in the intervention group and 49 patients in the control group completed the study (Fig.1).

In this study, explanatory variables included: (i) age which was divided into 20-39, 40-59 and 60- group, (ii) marriage (unmarried, married, divorced, widowhood), (iii) education level (primary school or lower, junior school, high school and college and above), (iv) household income per month (≤ 2000 , 2000-5000 and ≥ 5000), (v) medical insurance (no, rural cooperation medical service, and other insurance), (vi) profession (unemployed, working at the job, retirement), (vii) clinical TNM stages (I stage, II stage, III stage), (viii) Chemotherapy regimens (AC sequential Paclitaxel or Docetaxel, TEC or TC, Other) and (ix) side effects of chemotherapy (mild, moderate, severe). In the study, intervention variable (intervention group and control group) and time variable (baseline, the first, the third and the sixth chemotherapy) were involved.

The primary endpoint was the change in the score of PSQI-total from baseline with the secondary endpoints being the changes in the components of PSQI-total (sleep quality, fall-asleep time, sleep duration, sleep efficiency, sleep disturbance, use of sleep medication, daytime function) from baseline. A linear mixed model taking account of repeated measurements was used to assess the effect of music therapy combined with aerobic exercise intervention on the sleep quality after controlling for all the explanatory variables and the interaction of intervention variable and time variable.

Data was entered twice into Epidata Version 3.0 software (CDC, Atlanta, GA, USA) and all statistical analysis was performed using SAS 9.4 ((Statistics Analysis System, Inc. Cary, North Carolina, USA). The significance was achieved from statistical tests when $P < 0.05$.

Result

Baseline characteristics

A total of 100 eligible participants were involved into this study. The average age of them was 44.73 ± 11.697 years ranged from 25 to 71 years old. These participants at the age of 40 to 59 years old accounted for 51%, and there was a percentage of 86% of the married participants.

In addition, the income of roughly 21% of households had more than 5000 RMB each month. Medical insurance, including rural cooperative medical service, urban medical insurance, social insurance, commercial insurance, covered 99% of patients. It was found that around 63% of patients have permanent jobs. The patients with breast cancer at I stages of clinical TNM stages reach 66%. Meanwhile, 88% of patients received chemotherapy had moderate side effects in the course of chemotherapy.

Results indicated that there were not significant differences between the intervention group and the control group in age, marriage, education level, households income, profession, Medical insurance, cancer clinical TNM stages, course of chemotherapy treatment, and severity of side effect of chemotherapy ($P \geq 0.05$) (Table 1).

Table 1
Baseline characteristics of patients with breast cancer

Baseline characteristics	Total number		Experimental group		Control group		χ^2	P
	(n = 100)		(n = 51)		(n = 49)			
	n	%	n	%	n	%		
Age (year) (mean \pm SD)	44.73 \pm 11.697		44.47 \pm 11.399		45.00 \pm 12.112			
Age(year)							1.410	0.494
20–39	33	33.0	18	35.3	15	30.6		
40–59	51	51.0	27	52.9	24	49.0		
60-	16	16.0	6	11.8	10	20.4		
Marriage							1.207	0.751
Unmarried	5	5.0	3	5.9	2	4.1		
Married	86	86.0	42	82.4	44	89.8		
Divorced	6	6.0	4	7.8	2	4.1		
Widowhood	3	3.0	2	3.9	1	2.0		
Education level							3.597	0.308
Primary school or lower	19	19.0	8	15.7	11	22.4		
Junior school	20	20.0	13	25.5	7	14.3		
High school	32	32.0	18	35.3	14	28.6		
College and above	29	29.0	12	23.5	17	34.7		
Household income per month							0.713	0.700
\leq 2000	26	26.0	14	27.5	12	24.5		
2000–5000	53	53.0	25	49.0	28	57.1		
\geq 5000	21	21.0	12	23.5	9	18.4		
Medical insurance							1.827	0.401
no	1	1.0	0	0	1	2.0		
Rural cooperation medical service	54	54.0	30	58.8	24	49.0		
Other insurance	45	45.0	21	41.2	24	49.0		
Profession							0.428	0.807
Unemployed	32	32.0	15	29.4	17	34.7		
Working at the job	63	63.0	33	64.7	30	61.2		
Retirement	5	5.0	3	5.9	2	4.1		
Clinical TNM stages							0.675	0.714
Ⅱstage	8	8.0	5	9.8	3	6.1		

Baseline characteristics	Total number (n = 100)		Experimental group (n = 51)		Control group (n = 49)		χ^2	P
	n	%	n	%	n	%		
	Stage	66	66.0	32	62.7	34		
Stage	26	26	14	27.5	12	24.5		
Side effects of chemotherapy							0.450	0.798
Mild	9	9.0	4	7.8	5	10.2		
Moderate	88	88.0	45	88.2	43	87.8		
Severe	3	3.0	2	3.9	1	2.0		
Chemotherapy regimens							0.361	0.835
AC sequential Paclitaxel or Docetaxel	24	24.0	13	25.5	11	22.4		
TEC or TC	50	50.0	26	51.0	24	49.0		
Other	26	26.0	12	23.5	14	28.6		

Sleep Quality Of Patients

The mean score of sleep quality of patients in 100 patients with breast cancer was 8.86 ± 2.34 on the 10th day after radical mastectomy. In this study, patients with PSQI total score greater than 7 points were considered as sleep problem. Results indicated that approximately 89% of patients suffered from sleep problem. Each dimension of PSQI with the score greater than 2 points was suggested to be poor. According to the result of this study, 56% of patients had the problem of poor subjective sleep quality; 42.0% of patients had the trouble in falling asleep; 34% of patients had sleep disturbance (easy to get up, get up early, frequently to go toilet at night). About 34% of patients slept less than 6 hours, and had daytime dysfunction such as energy shortage and fatigue (Table 2).

Table 2
The score of Pittsburgh Sleep Quality Index among patients

	Full score	Min	Max	Score \geq 2 (%)	M \pm SD	The national average [20]	P
Total	23	3	18		8.86 \pm 2.34	3.88 \pm 2.52	< 0.001
Subjective sleep quality	3	0	3	56.0	1.71 \pm 0.74	0.63 \pm 0.68	< 0.001
Fall-asleep time	3	0	3	42.0	1.49 \pm 0.66	0.70 \pm 0.86	< 0.001
Sleep duration	3	0	3	34.0	1.34 \pm 0.77	0.70 \pm 0.58	< 0.001
Sleep efficiency	3	0	3	38.0	1.43 \pm 0.62	0.15 \pm 0.47	< 0.001
Sleep disturbance	3	0	3	34.0	1.42 \pm 0.73	0.90 \pm 0.44	< 0.001
Use of sleep medication	3	0	1	0.00	0.02 \pm 0.14	0.06 \pm 0.24	< 0.001
Daytime function	3	0	3	40.0	1.45 \pm 0.72	0.73 \pm 0.83	< 0.001

Change In Sleep Quality Scores

A linear mixed model was used to explore the effect of music therapy combined with aerobic exercise intervention on sleep quality, after adjusting for age, marriage, education level, profession, household income, medical insurance, cancer clinical TNM stages, and severity of side effect of chemotherapy. For the primary endpoints (PSQI-total), nonsignificant improvement was observed in the intervention group at the first post-test (difference between groups: -0.51; 95%CI: -1.25, 0.23). However, change in PSQI-total had increased from 1st post-test to 3rd post-test gradually increased in the intervention group (difference between groups: -1.31(-2.05, -0.57)to -2.10(-2.84, -1.36). On the contrary, significant increases in changes of the PSQI-total in control groups from 1st post-test to 3rd post-test was clear (difference between groups: 0.549 (-0.18, 1.28) to 2.745 (2.02, 3.47). With the prolongation of chemotherapy cycle, the total score of PSQI and the score of sleep quality factors in the intervention group showed a downward trend, while the total score of PSQI and the score of sleep quality factors in the control group showed an upward trend.

Significant improvements from baseline in all indices for sleep quality measurement were observed throughout the intervention period in both intervention and control groups from 1st post-test to 3rd post-test (Table 3). For these secondary endpoints, including sleep quality, fall-asleep time, sleep duration, sleep efficiency, sleep disturbance, daytime function, a similar trend to that observed with PSQI-total in two different groups did still persist.

Table 3
Results from mixed model analysis of change in sleep quality score from baseline

	Baseline (mean ± SD)	1st post- test (mean ± SD)	Change between baseline and 1st post-test (95% CI)	2nd post- test (mean ± SD)	Change between baseline and 2nd post-test (95% CI)	3rd post- test (mean ± SD)	Change between baseline and 3rd post-test (95% CI)
Intervention group	n = 55	n = 55		n = 53		n = 51	
Total	8.82 ± 2.09	8.27 ± 1.93	-0.51(-1.25,0.23)	7.24 ± 2.02	-1.31(-2.05,-0.57)	6.08 ± 1.61	-2.10(-2.84,-1.36)
Subjective sleep quality	1.73 ± 0.70	1.57 ± 0.64	-0.02(-0.29,0.25)	1.43 ± 0.78	-0.10(-0.37,0.17)	1.31 ± 0.47	-0.23(-0.49,0.04)
Fall-asleep time	1.43 ± 0.61	1.31 ± 0.68	-0.08(-0.35,0.19)	1.20 ± 0.89	-0.20(-0.48,0.07)	1.00 ± 0.60	-0.41(-0.68,-0.14)
Sleep duration	1.33 ± 0.62	1.16 ± 0.86	-0.04(-0.33,0.25)	1.00 ± 0.72	-0.18(-0.47,0.10)	0.84 ± 0.58	-0.51(-0.80,-0.22)
Sleep efficiency	1.41 ± 0.64	1.29 ± 0.73	-0.122(-0.39,0.15)	1.08 ± 0.66	-0.31(-0.57,-0.04)	0.88 ± 0.43	-0.41(-0.68,-0.14)
Sleep disturbance	1.41 ± 0.64	1.61 ± 0.96	-0.163(-0.48,0.15)	1.43 ± 0.92	-0.25(-0.56,0.07)	1.16 ± 0.58	-0.37(-0.68,-0.06)
Use of sleep medication	0.04 ± 0.20	0.02 ± 0.14	-0.020(-0.07,0.03)	0.00	-0.02(-0.07,0.03)	0.00	-0.02(-0.07,0.03)
Daytime function	1.47 ± 0.70	1.31 ± 0.99	-0.061(-0.36,0.24)	1.10 ± 0.81	-0.25(-0.55,0.06)	0.88 ± 0.68	-0.41(-0.71,-0.11)
Control group	n = 55	n = 55		n = 53		n = 49	
Total	8.90 ± 2.60	9.41 ± 2.00	0.549 (-0.18,1.28)	10.20 ± 1.93	1.59(0.86,2.31)	11.00 ± 2.10	2.75 (2.02,3.47)
Subjective sleep quality	1.69 ± 0.80	1.71 ± 0.71	0.16(-0.11,0.42)	1.80 ± 0.76	0.29(0.03,0.56)	1.92 ± 0.93	0.41(0.15,0.67)
Fall-asleep time	1.55 ± 0.71	1.63 ± 0.70	0.12(-0.15,0.38)	1.76 ± 0.75	0.24(-0.03,0.50)	1.96 ± 0.79	0.43(0.17,0.70)
Sleep duration	1.35 ± 0.90	1.39 ± 0.84	0.18(-0.10,0.46)	1.53 ± 0.62	0.33(0.05,0.61)	1.61 ± 0.79	0.45(0.17,0.73)
Sleep efficiency	1.45 ± 0.61	1.57 ± 0.65	0.12(-0.15,0.38)	1.76 ± 0.72	0.33(0.07,0.60)	1.86 ± 0.89	0.53(0.27,0.79)
Sleep disturbance	1.43 ± 0.82	1.59 ± 0.73	-0.20(-0.50,0.11)	1.67 ± 0.80	-0.02(-0.33,0.29)	1.80 ± 0.82	0.26(0.29,0.56)
Use of sleep medication	0	0.02 ± 0.14	0.02(-0.03,0.07)	0.02 ± 0.14	0.04(-0.01,0.09)	0.02 ± 0.14	0.04(-0.01,0.09)
Daytime function	1.43 ± 0 .74	1.49 ± 0.71	0.16(-0.14,0.45)	1.67 ± 0.82	0.37(0.08,0.67)	1.84 ± 0.77	0.59(0.29,0.88)

Note: Mixed model was used for the analysis of change in sleep quality score from baseline with baseline measurement of age, marriage, household income, medical insurance, profession, clinical TNM stages, course of chemotherapy treatment, side effects of chemotherapy as covariate, intervention, time, treatment and time interaction as fixed effects, and patient as random effect.

Discussion

In the Randomized controlled trial of music therapy combined with aerobic exercise intervention, we found that sleep quality of female breast cancer patients on chemotherapy after radical mastectomy was worse compared with the Chinese average. And there are problems in subjective sleep quality, fall-asleep time, sleep duration, sleep efficiency, daytime function and so on. After the music therapy combined with aerobic exercise intervention, significant improvements in terms of PSQI-total score, subjective sleep quality, fall-asleep time, sleep duration, sleep efficiency, sleep disturbance, daytime function could be observed. These results suggested that music therapy combined with aerobic exercise is a feasible and effective, non-pharmacological method, which could significantly improve the sleep quality of breast cancer patients on chemotherapy after radical mastectomy.

Sleep quality of breast cancer patients on chemotherapy after radical mastectomy

Due to radical mastectomy of female breast cancer patients making their breast incomplete, changing female characteristic and influencing their role in the family, along with side effect of chemotherapy and large economic burden, patients often suffered from psychological, physiological and social disorders. Thus, negative emotions such as anxiety and depression, often accompanied them and decreased the sleep quality of patients [21].

In this study, the mean PSQI total score of the participants was 8.86 ± 2.34 , which was higher than the national level in China (3.88 ± 2.52) [20] and the level of breast cancer patients in Fortner's study (6.8 ± 4.0) [21], but was below results of insomniacs in Buysse's study (10.38 ± 4.57) [19].

The result in our study showed that patients suffered from sleep problem accounted for 89.0% suggesting the sleep problem was the common problem of breast cancer patients on chemotherapy after radical mastectomy. This was similar to that of Holley's study on the incidence of sleep disorders in patients with breast cancer by more than 90% [22]. Research from Fortner indicated that the proportion of patients suffering from sleep problem reached approximately 61% [23]. Of metastatic breast cancer (MBC) patients in the study conducted by Koopman approximately 63% had one or more kinds of sleep problems [24]. Paresh also confirmed that sleep problem is the common symptom of breast cancer patients, with sleep disturbance occurring among about 64% of patients [25]. Further, a study in China carried out by Xue Shuying showed that approximately 63.04% of breast cancer patients after radical mastectomy were subjected to sleep problem of different degree [26].

Compared to the research results above, the proportion of sleep problem appeared to be higher among breast cancer patients on chemotherapy after radical mastectomy in our study. We speculated that the discrepancies may be attributed to the patient's age, economic conditions, medical payment mode, clinical stage of tumor and the severity of side effects of chemotherapy and measuring method.

Music therapy combined with aerobic exercise intervention on the sleep quality of patients

The sleep disorder is one of the most common symptoms of the patients after radical operation of the breast cancer, which seriously affects the outcome, physical and mental health and the quality of life of the patients, and the sleep disorder is often associated with the symptoms of anxiety, depression, cancer fatigue, pain and the like, so that the immunity of the body can be reduced, Severe sleep disorders and increased risk of breast cancer [6, 27–28].

With the change of the surgical treatment and the systematic treatment scheme of the breast cancer, the death rate of the patient is reduced by 25%, and the problems of muscle atrophy and joint contracture are apt to occur after the operation, and the normal function of the affected limb, in particular the shoulder joint, is affected, And the toxic and side effect of the chemotherapy greatly reduces the quality of life of the patient. Therefore, it is very important for cancer patients to find an effective way to improve sleep disorder and improve their quality of life.

This study showed that music therapy combined with aerobic exercise reduced the PSQI-total scores significantly at the post-tests. Significant improvements from baseline in all indices for sleep quality measurement were also observed throughout the intervention period in both intervention and control groups from 1st post-test to 3rd post-test.

This study conforms to the change of modern medical model, aiming at all kinds of negative effects on patients after radical mastectomy, comprehensive rehabilitation intervention from three aspects of patients' limb function, psychological and social adaptability, music therapy combined with aerobic exercise, and according to the three stages of postoperative chemotherapy for patients with breast cancer, a scientific, standardized and individualized exercise prescription for patients. Guide patients to carry out systematic rehabilitation training during chemotherapy, so that the sleep quality of patients can be significantly improved.

Music therapy, which is based on medical psychology, is a kind of non-invasive, natural therapy. Through beautiful and harmonious music, patients have emotional and psychological effects, and achieve empathy, suggestion, induction and other therapeutic effects in psychology [29]. It can effectively relax the stress of the cancer patient, let the patient walk into the beautiful music, temporarily forget the environment of the body, make the patient relax, improve the mental state, and thus promote the sleep [30].

Some studies have shown that music therapy can relieve mild to moderate pain, effectively alleviate the poor sleep quality caused by negative emotions such as depression, fear, anxiety and depression in cancer patients, and can also interfere with the release of substances such as morphine tie, play a sedative, hypnotic effect, and then improve sleep quality [11, 31–32]. Other studies have shown that music therapy can relieve symptoms that interfere with the daily life of cancer patients, such as fatigue, nausea and sleep disorders [33, 34]. Music therapy enables people to experience music, to eliminate psychological obstacles, to restore or improve mental and physical health, and to improve the quality of life [35].

The American Cancer Prevention Association has confirmed that aerobic exercise is one of the most effective ways to fight cancer and prevent cancer. It can effectively reverse the depression of cancer patients after illness, relieve tension and improve the function of the immune system of the human body [36]. Aerobic exercise has also been proved to be one of the main interventions to improve the overall quality of life of patients with breast cancer, which can not only reduce the mortality of cancer, but also help patients recover [37–38].

A large number of studies have shown that aerobic exercise is regarded as a non-pharmaceutical form of behavioral intervention, similar to systemic relaxation, image and relaxation therapy, which can promote the recovery of upper limb function, prevent the occurrence of lymphedema, improve cardiopulmonary function, relieve psychological stress, reduce cancer-related fatigue, reduce chemotherapy-related nausea, control weight, and improve the social support status of patients with breast cancer [39–40].

The largest strength of our study was the design procedure of controlled random trial. Thus, the cause-effect relationship was able to be clearly confirmed. Although large efforts had been made to perfect our study, we still have to knowledge some limitations in the study. Firstly, the data were self-reported and could be influenced by many potential factors, such as defensiveness, misrepresentation, personal emotions, and attitudes. Secondly, no biomarkers or physiological measurements were done, which need to be further explored. What's more, our study results were likely to

be subjected to the low sample size. Finally, because of only one study hospitals in the study, the present findings are likely to have a low degree of generalizability to other areas in China. In spite of the limitations above, this is the first study of exploring the effect of music therapy combined with aerobic exercise with a high popularity in China on breast cancer patients during the course of chemotherapy after radical mastectomy.

In conclusion, according to the results through the randomized controlled trial, sleep disorder was one of the most common symptoms of breast cancer patients during the course of chemotherapy after radical mastectomy. The PSQI-total scores had decreased after the 6th chemotherapy in the intervention group. With the increase of chemotherapy cycle, the total score of PSQI and the score of sleep quality in the intervention group showed a decreasing trend. Significant improvements from baseline in all indices for sleep quality measurement were observed throughout the intervention period.

Music therapy combined with aerobic exercise is low-cost, convenient, safe, effective and easily techniques to improve the sleep quality of patients obviously. Surely, further research and more experience of music therapy combined with aerobic exercise are still needed. In the practice of clinical nursing, the preference of the patient to the music, the stress tolerance of the patient and the degree of upper limb activity of the affected side should be comprehensively evaluated.

Declarations

Ethics approval and consent to participate

The protocol was reviewed and approved by the Human Research Ethics Committee of Shaanxi Provincial Tumor Hospital, and informed consent was obtained from all participants or their families.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analyzed during this study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no conflicts of interest.

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Author Contributions

LC and XL conceived and designed the experiments. LC, YW, JZ did the intervention interview and collected the data. WZ and LY analyzed the data. LC drafted the paper. All authors participated in editing and approved the final manuscript.

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Figures

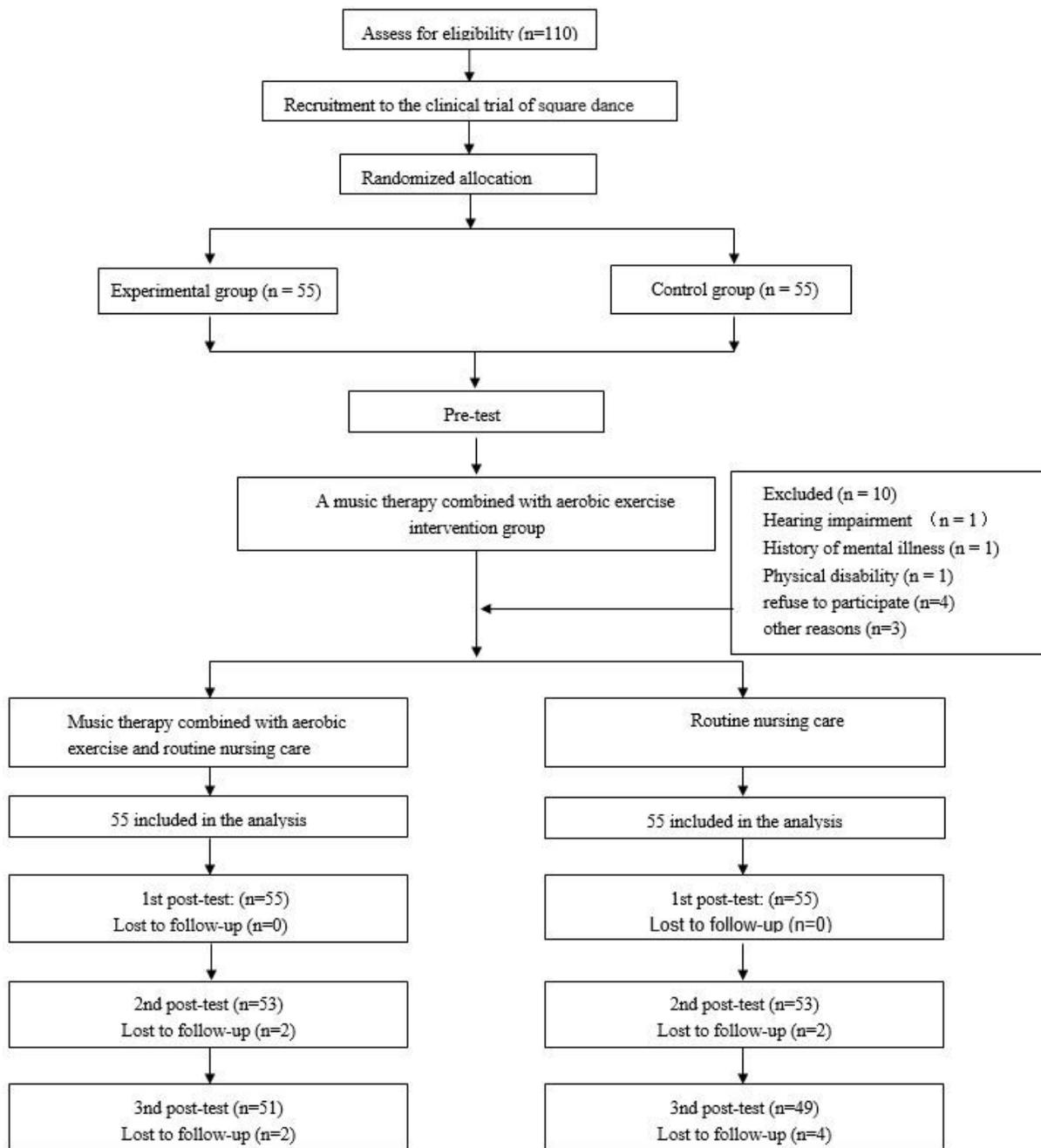


Figure 1

Flow chart of the study