Promoting Physical and Psychological Rehabilitation Activities and Evaluating Potential Links Among Cancer-Related Fatigue, Fear of Recurrence, Quality of Life, and Physiological Indicators in Cancer Survivors

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Abstract

Objectives: Cancer-related fatigue and fear of recurrence (FOR) are the most common symptoms in cancer survivors and severely affect quality of life (QOL). This study aims to promote and evaluate the effectiveness of physical and psychological rehabilitation activities for cancer survivors. **Methods:** A longitudinal study with an interventional research design was conducted. A total of 80 participants were randomly assigned to experimental groups E1 (Qigong exercise [QE]) or E2 (stress management [SM]) or the control group. The E1 and E2 groups received QE and SM, respectively, as interventions once a week for 12 weeks, and effects were assessed. Cancer-related fatigue, FOR, QOL, and heart rate variability (HRV) were evaluated at baseline (T0), after 12 weeks (T1), and at the 3-month follow-up (T2). **Results:** QE and SM effectively strengthened the physical and psychological functions of cancer survivors at the T1 phase. Although differences in FOR and QOL were not statistically significant, the scores were decreased and increased, respectively. Although the effects during the T2 phase were not as significant as those during T1, the score progress was maintained. The effects on HRV were significantly different among the E1, E2, and control groups at T1, which shows that the performance of both experimental groups was better than that of the control group. **Conclusions:** Physical and psychological rehabilitation activities should be practiced periodically and should be led by professional staff. Long-term educational resources and care should also be provided. HRV can be used to efficiently monitor the status of the mind-body balance and is a more suitable index than questionnaires for physical and psychological function evaluation in cancer survivors.

Keywords

cancer survivors, cancer-related fatigue, fear of recurrence, quality of life, heart rate variability, Qigong exercise, stress management

Introduction

According to the Global Burden of Disease Report, cancer is the second leading cause of death worldwide. In the past 10 years, the incidence of cancer has increased by 33%. Thus, cancer poses a great threat to the health of humanity.[1] Cancer-related fatigue (CRF) and fear of recurrence (FOR) are common seriously disturbing problems faced by cancer survivors.[2-4] CRF is accompanied by lack of strength, depressed mood, and sleep disorders, which lead to reduced physical, social, cognitive, and vocational

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function. Moreover, CRF can easily be overlooked by medical staff, resulting in delayed treatment.[5,6]

Cancer recurrence is the most difficult stage during the course of the disease. FOR can lead to emotional distress and cognitive and behavioral disorders that can affect recovery. FOR does not decrease as the treatment ends or as the survival duration increases. Patients with a good prognosis or a low risk of recurrence remain fearful or worried, which severely affects their quality of life (QOL) and results in burdens to the individual, family, and society.[7] Approximately one third of cancer survivors suffer from the long-term impact of CRF,[8] and more than 70% are currently experiencing FOR.[9,10]

Cancer-related physical and physiological disorders can cause autonomic nervous system (ANS) dysfunction. Compared with healthy individuals, cancer survivors generally have lower heart rate variability (HRV).[11-13] HRV can be used to monitor the regulatory functions and status of the human ANS.[13] In clinical practice, HRV has not only been adopted as a diagnostic indicator of ANS dysfunction[14] but has also been used as a marker for cancer-related distress and recovery status.[12]

Cancer survivors must tolerate pain caused by the disease and are also under greater psychological pressures than other people. The influence of the mind-body interaction leads to decreased physical functions and can even diminish the effects of medical treatments. In recent years, more than 75% of cancer survivors have undergone traditional cancer treatment in combination with complementary and alternative medicine to reduce the disturbing symptoms of cancer. This integrative treatment has yielded improved effects and increased QOL.[15,16] Some studies have shown that 12 weeks of Qigong exercise (QE) intervention can reduce fatigue, anxiety, and depression and promote quality of sleep in breast and prostate cancer patients.[17-19] Therefore, this study adopted "Guide health-preserving Qigong" as a QE intervention. QE, which is widely applied in complementary and alternative medicine, can increase blood circulation, improve lung and heart function, regulate homeostasis, moderate emotions, and allow self-healing.[20-22]

Some research has indicated that participation in stress management (SM) training courses may promote life value, self-efficacy, and QOL and may reduce the physical and mental symptoms of cancer patients.[3,6,23] SM helps cancer survivors realize the value of life, seek self-development, and improve their interpersonal relationships.[3,23,24] Hence, QE and SM can both promote the self-regulation functions of the body, improve HRV, and restore balance to the ANS.[11,25-27] Furthermore, QE and SM can alleviate symptoms such as fatigue, anxiety, depression, and sleep disorders and can thus improve the QOL of cancer survivors.[18,27-31] After regular treatments, providing cancer survivors with immediate and effective interventions during the recovery stage to assist in reducing distress due to the mental and physical symptoms of the disease is necessary and urgent. The results of this study can assist cancer survivors in maintaining recovery activities and restoring QOL and can provide a reference for care following treatment for cancer.

Methods

A longitudinal study with an interventional research design was conducted separately in 2 cancer centers in northern and southern Taiwan. The participants were randomly assigned to experimental groups E1 (QE) or E2 (SM) or to the control group. A 12-week intervention and a 3-month follow-up evaluation were employed in this study.

Participants and Study Design

Eligibility Criteria. The inclusion criteria for the participants were cancer survivors who (1) had completed regular treatment, including surgery, chemotherapy, radiation therapy, and target therapy, at least 1 month prior to the beginning of the study; (2) had experienced no cancer recurrence; and (3) had received hormone replacement therapy for breast cancer. The exclusion criteria were (1) participants with a diagnosis of stage IV cancer; and (2) participants with moderate or severe arrhythmia.

Sample Size. The medium effect sizes recommended in relevant studies before and after implementing intervention and during follow-up were adopted for the sample calculation.[18] Repeated-measures analysis of variance (ANOVA) was performed using G*Power software. The effect size was 0.3, the α was 0.05, and the power was 0.8. The expected dropout rate was 25%. Thus, a minimum of 98 participants was required for this study. There were 99 qualified participants recruited from the 2 cancer centers. The participants were randomly assigned to the QE group (E1 = 33), the SM group (E2 = 33), or the control group (n = 33). However, only 80 participants completed the intervention. Twenty-nine of these were in the E1 group (n = 29), 25 were in the E2 group (n = 25), and 26 were in the control group (n = 26; Figure 1).

Study Design. Prior to the intervention, a 2-hour basic nutrition management course was provided to all participants. Subsequently, the E1 group received QE training, and the E2 group received SM training. The intervention was conducted once a week for 2 hours for a total of 12 weeks. No intervention was performed in the control group; the participants in that group maintained their daily routines. Data for overall CRF, FOR, the QOL questionnaire, and HRV were collected at 3 time points at 3-month intervals. The time points used to assess the potential improvement were baseline (T0), 12 weeks postintervention (T1), and 3-month follow-up (T2).
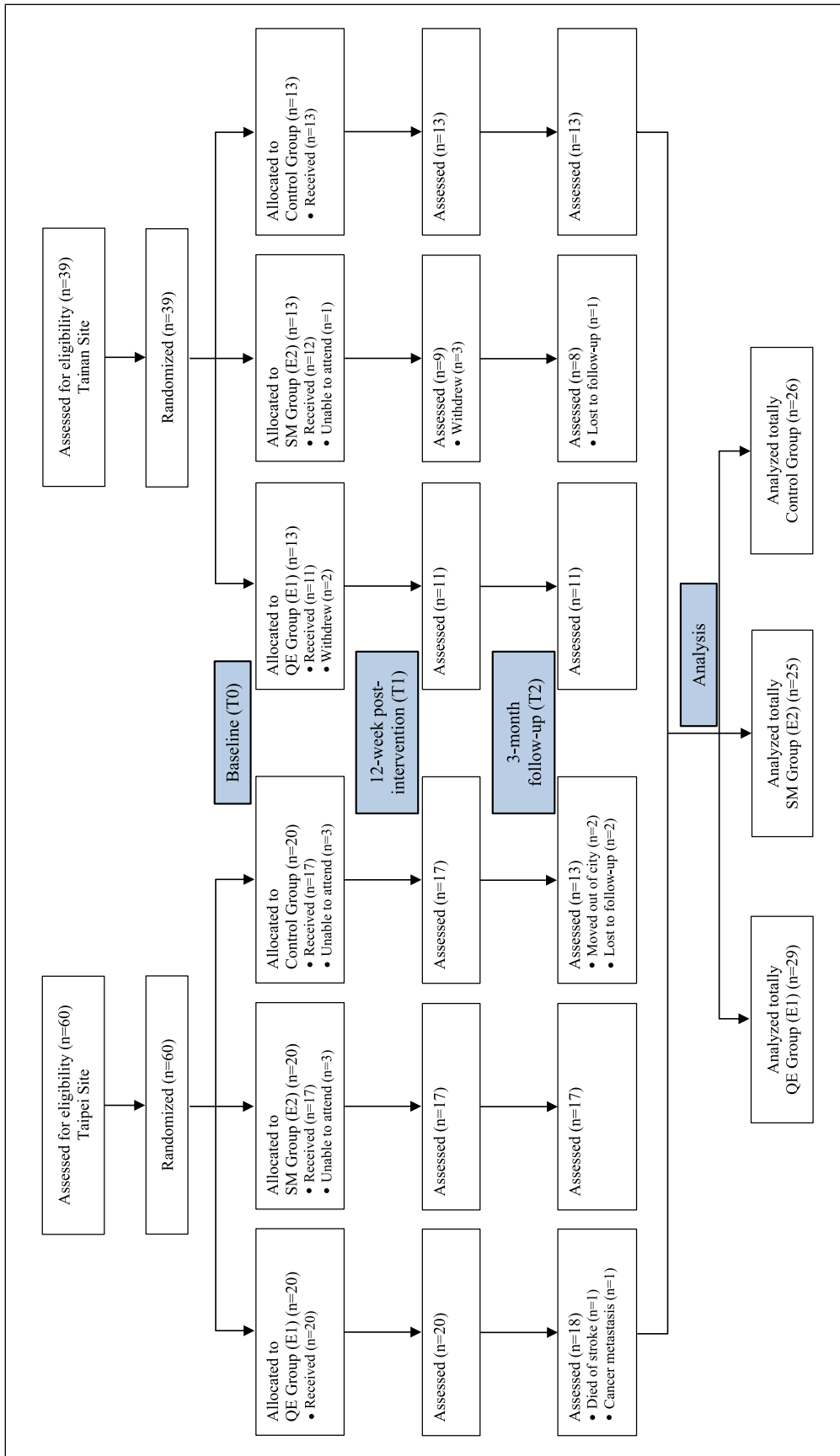
Figure 1. CONSORT flow diagram of this study.

Assessed for eligibility (n=60)
Taipei Site

Randomized (n=60)

Allocated to
QE Group (E1) (n=20)
• Received (n=20)

Allocated to
SM Group (E2) (n=20)
• Received (n=17)
• Unable to attend (n=3)

Allocated to
Control Group (n=20)
• Received (n=17)
• Unable to attend (n=3)

Assessed (n=20)

Assessed (n=17)

Assessed (n=17)

Assessed (n=18)
• Died of stroke (n=1)
• Cancer metastasis (n=1)

Assessed (n=17)

Assessed (n=13)
• Moved out of city (n=2)
• Lost to follow-up (n=2)

Assessed for eligibility (n=39)
Tainan Site

Randomized (n=39)

Allocated to
QE Group (E1) (n=13)
• Received (n=11)
• Withdrew (n=2)

Allocated to
SM Group (E2) (n=13)
• Received (n=12)
• Unable to attend (n=1)

Allocated to
Control Group (n=13)
• Received (n=13)

Assessed (n=11)

Assessed (n=9)
• Withdrew (n=3)

Assessed (n=13)

Assessed (n=11)

Assessed (n=8)
• Lost to follow-up (n=1)

Assessed (n=13)

Baseline (T0)

12-week post-
intervention (T1)

3-month
follow-up (T2)

Analysis

Analyzed totally
QE Group (E1) (n=29)

Analyzed totally
SM Group (E2) (n=25)

Analyzed totally
Control Group (n=26)

1185

Outcome Measures

A pilot study was conducted by performing pretesting on 99 cancer patients in outpatient clinics to verify the reliability and validity of the CRF and FOR scales.

CRF Scale. The CRF scale was designed based on the diagnosis criteria of the ICD-10 (International Classification of Diseases, Tenth Revision) and included 15 items.[32] A 5-point Likert-type scale was utilized for all items used to evaluate the degree of fatigue of cancer survivors within the past 2 weeks. Higher scores indicated severe CRF. Exploratory factor analysis was adopted. Factor loadings were evaluated using the maximum likelihood method; the Kaiser-Meyer-Olkin value was 0.839. Bartlett's test of sphericity yielded $\chi^2 = 541.686$ ($P < .001$). Finally, principal component analysis with axis rotation was applied to examine the construct validity of the scale. Factors with eigenvalues >1 were extracted, and only 10 questions remained after multiple examinations. The 10 questions can be categorized into 3 domains: lifestyle function, mind-body function, and sleep condition. The accumulated variation was 74.998%. The overall Cronbach's α of the internal consistency reliability of the scale was 0.878, suggesting very good reliability and effectiveness. Moreover, within each domain, the correlation coefficient of each item was greater than 0.500 after removing the question, indicating good reliability and effectiveness of the questionnaire as a measurement tool for evaluating CRF (Table 1).

FOR Scale. The FOR scale was designed based on the Chinese edition of the Fear of Cancer Recurrence Inventory (FCRI) and included 42 items. A 5-point Likert-type scale was utilized for all items used to evaluate the degree of fear of cancer recurrence among the cancer survivors during the past month; higher scores indicated more severe FOR.[33] Exploratory factor analysis and verification were performed. The Kaiser-Meyer-Olkin value was 0.915, and Bartlett's test of sphericity yielded $\chi^2 = 1254.630$ ($P < .001$). Only 15 questions were retained, and they were categorized into 3 domains: psychological distress, lifestyle function, and triggers. The accumulated variation was 79.073%. The overall Cronbach's α of the internal consistency reliability of the scale was 0.954, suggesting very good reliability and effectiveness. Moreover, within each area, the correlation coefficient of each item was greater than 0.500 after removing the question. The results indicate that the questionnaire was reliable and effective as a measurement tool for evaluating FOR (Table 1).

QOL Scale. The QOL scale was designed based on the fourth Chinese edition of the Functional Assessment of Cancer Therapy-General (FACT-G) and included 27 items.

The original English version contained 28 questions. To improve the internal consistency and stability of the theme, the construct validity factor analysis and verification were performed again. A total of 4 component themes were selected, and the scale was finally reduced to 27 questions, becoming the fourth edition of the Chinese version of the FACT-G scale. A 5-point Likert-type scale was utilized for all items used to examine the level of QOL within the past 7 days. Four domains were included in the scale. The questions of physical and emotional well-being were reverse-scored. Higher scores indicated poorer QOL. For social/family and functional well-being, higher scores indicated higher life functions and better QOL.[34]

HRV Indicators. The CheckMyHeart Handel HRV, which has received safety certification from the Food and Drug Administration of the United States and the CE marking of the European Economic Area, was adapted for HRV examination. Participants were asked to avoid foods with intense flavors, smoking, and caffeinated and alcoholic beverages the day before the test.[35] The room temperature was maintained at 23°C to 25°C. The participants were seated or lying prone during a 5-minute Lead II electrocardiography recording. The recorded data were converted to HRV indicators using time domain and frequency domain analysis methods as described below:

1. Standard deviation of normal R-R intervals (SDNN) represents the overall activity of HRV in the time domain; a higher score indicates higher HRV overall activity.
2. Total power (TP): the clinical meaning of TP in the frequency domain is similar to that of SDNN in the time domain; a lower score indicates a higher level of fatigue, a lack of energy, or a lack of strength.
3. High frequency (HF) represents the parasympathetic nervous system activity in the frequency domain; a lower score indicates that the subject is experiencing anxiety or stress, whereas a higher score indicates relaxation.

Interventions

Mind-body support and social support are indispensable components of education and care for cancer patients. The Memorial Sloan-Kettering Cancer Center and the MD Anderson Cancer Center in the United States actively promote mind-body support treatment, and such treatment has become part of the traditional cancer treatment method.[36,37] Moreover, provision of balanced nutrition and supplements is considered critical in the care of cancer survivors. Therefore, CRF, FOR, QOL, and HRV were monitored to evaluate the effects of physical and psychological activities as interventions.

Table 1. A Pilot Study for Factor Analysis of Cancer-Related Fatigue and Fear of Recurrence Scales.

| | Factor | | |
| | 1 | 2 | 3 |
Cancer-Related Fatigue (CRF)	Lifestyle Function	Mind-Body Function	Sleep Condition
Difficulty completing daily tasks attributed to feeling fatigued	0.855		
Significant diminished energy in daily life or social of functioning	0.811		
Decreased motivation or interest to engage in usual activities	0.768		
Perceived need to struggle to overcome inactivity	0.750		
Perceived problems with short-term memory		0.865	
Diminished concentration or attention		0.845	
Complaints of generalized weakness or limb heaviness		0.750	
Post-exertional malaise lasting several hours		0.667	
Hypersomnia			0.893
Experience of sleep as unrefreshing or nonrestorative			0.796
Cronbach's α:			
Factor 1 = 0.873		KMO = 0.839, χ^2 = 541.686***	
Factor 2 = 0.864		Total variance explained 87.8%	
Factor 3 = 0.715			

| | Factor | | |
| | 1 | 2 | 3 |
Fear of Recurrence (FOR)	Psychological Distress	Lifestyle Function	Triggers
Sadness, discouragement, or disappointment	0.858		
Worry, fear, or anxiety	0.833		
Helplessness or resignation	0.780		
Frustration, anger, or outrage	0.779		
I am worried or anxious about the FOR	0.774		
I am afraid of a cancer recurrence	0.768		
When I think about FOR, other unpleasant thoughts or images come to mind (death, suffering consequences for my family)	0.748		
My social or leisure activities (eg, outings, sports, travel)		0.880	
My work or everyday activities		0.866	
My relationship with my partner, my family, or those close to me		0.836	
My quality of life in general		0.762	
My ability to make future plans or set life goals		0.690	
Seeing or hearing someone who is ill			0.859
Going to funeral or reading the obituary section of the paper			0.768
Television shows or newspaper articles about cancer or illness			0.684
Cronbach's α:			
Factor 1 = 0.956		KMO = 0.915, χ^2 = 1254.630***	
Factor 2 = 0.936		Total variance explained 95.4%	
Factor 3 = 0.794			

Abbreviations: KMO, Kaiser-Meyer-Olkin.
***$P < .001$

Nutrition Management. Two hours of nutrition management education were provided to the 3 groups of participants by a certified dietitian. Accurate dietary principles were introduced, and dietary habits were adjusted to achieve a balanced diet and to supply adequate nutrition.

Qigong Exercise. A certified martial arts specialist of the International Wushu Federation taught the method of 12-style QE, including standing position, meditation, and leg massage. The exercises allow enhancement of heart and lung function, facilitate blood and energy circulation,

regulate physical functions, allow deep relaxation of the body, and promote self-healing capabilities. Handouts and demonstration DVDs were provided to encourage the participants to practice at home and to improve their skills.

Stress management. A rehabilitation and mental health counseling professor led the patients in the SM group. The program involved conversation and sharing of cognitive behavior modification and mindfulness decompression for a total of 90 minutes. During the remaining 20 minutes, body relaxation and meditation techniques that patients could use to relieve mental and emotional stress were demonstrated. The cognitive behavior modification process was divided into 3 phases as follows[38]:

1. The first phase was "self-observation." During this phase, the patients learned how to perceive their behavior, listen to their inner voice, and develop a new viewpoint on their problems.
2. The second phase was "starting a new internal dialogue." In this phase, the patients learned to change their inappropriate inner dialogue and were helped restructure their cognition.
3. The third phase was "learning new skills." In this phase, the patients were taught effective response skills, how to use these skills to deal with pressure in life situations, and how to maintain these skills.

Data Analyses

The data were analyzed using SPSS 22.0 for Windows (SPSS Inc, Chicago, IL). Chi-square tests were used for comparisons of baseline categorical data among E1, E2, and the control group. The paired sample *t* test was used to compare the improvement effects of single interventions, and 1-way ANOVA was used to analyze the differences in effects among groups. The AR (1) model in the generalized estimating equation was determined to be the best model by QIC (quasi-information criterion) value and was implemented to evaluate correlations among the 3 time points as a basis for assessing improvement over time.

Results

Demographic Characteristics

Among the 80 study participants, there were more females (n = 70) than males (n = 10); the age of the participants ranged from 33 to 75 years, and 47.5% were between 50 and 59 years of age. The cancer survival period ranged from 1.1 to 14.2 years, and 30.1% of the participants had survived for more than 5 years. The most frequent type of cancer among the participants was breast cancer (65%), and most cancers were at stage I or

II (72.6%) at diagnosis. A total of 56.3% of the participants felt fatigue, and approximately 25% experienced anxiety or depression. According to baseline (T0) data, almost all participants suffered from CRF (100%) and FOR (98.7%). In total, 77.5% had moderate or severe levels of fatigue, 47.5% suffered from moderate to severe emotional distress, and 7.5% experienced severe fatigue along with a tendency toward emotional distress. With the exception of the survival period, no significant differences in demographic characteristics were found among the 3 groups (Table 2).

Outcome Evaluations

Improvement Effects of Single Interventions. The results of paired sample *t* tests for single interventions are shown in Table 3. After 12 weeks of both QE and SM training (T1 vs T0), CRF was significantly reduced, whereas significant increases were observed for SDNN, TP, and HF. After a 3-month follow-up (T2 vs T0), continuous improvement was observed for CRF ($P < .05$), but significant decreases (T2 vs T1) were observed for SDNN and TP. Nevertheless, nonsignificant trends toward improvement were observed in FOR and QOL. Although FOR and QOL were not significantly decreased ($P > .05$), the FOR score was decreased, and the QOL score gradually increased.

The control group received only nutrition guidance. After 12 weeks (T1 vs T0), the control group participants had increased CRF, FOR and decreased QOL, SDNN, and TP. Only HF showed a slight increase ($t = 0.221$, $P = .827$). After 3 months of follow-up (T2 vs T0), FOR, QOL, SDNN, and HF showed gradual improvement; however, the changes were not significant ($P > .05$), and the participants remained affected by CRF ($t = 0.122$, $P = .903$) and TP ($t = -0.103$, $P = .919$). This result indicates that an appropriate intervention was crucial to managing participants' fatigue, emotional distress, and functional decline in ANS.

Between-Group Effects. One-way ANOVA between T1 versus T0 and T2 versus T0 showed that there were significant differences between E1, E2, and the control group at T1 in SDNN (T1-T0: F = 9.332, $P < .001$) and TP (T1-T0: F = 7.307, $P = .001$; Table 3).

Improvement Over Time. For generalized estimating equation, T0 was specified as the baseline category, and the control group was considered the reference group. At T1, CRF (T1: $\chi^2 = 5.344$, $P = .021$), SDNN (T1: $\chi^2 = 19.682$, $P < .001$), TP (T1: $\chi^2 = 10.616$, $P = .001$), and HF (T1: $\chi^2 = 6.391$, $P = .011$) all showed significant improvement ($P < .05$). CRF (T2: $\chi^2 = 4.777$, $P = .029$) still showed significant improvement at T2 ($P < .05$; Table 4).

Table 2. Demographic Characteristics of Participants at Baseline.

Characteristics	Frequency Distribution (%)				χ^2 Test	P
	E1 (n = 29)	E2 (n = 25)	Control (n = 26)	Total (N = 80)		
Gender					0.705	.703
Male	4 (13.8%)	2 (8.0%)	4 (15.4%)	10 (12.5%)		
Female	25 (86.2%)	23 (92.0%)	22 (84.6%)	70 (87.5%)		
Age (years)					3.848	.871
30-39	3 (10.3%)	1 (4.0%)	1 (3.8%)	5 (6.3%)		
40-49	7 (24.1%)	6 (24.0%)	5 (19.2%)	18 (22.5%)		
50-59	11 (37.9%)	12 (48.0%)	15 (57.7%)	38 (47.5%)		
60-69	5 (17.2%)	5 (20.0%)	3 (11.5%)	13 (16.3%)		
70-75	3 (10.3%)	1 (4.0%)	2 (7.7%)	6 (7.5%)		
Marital status					7.013	.535
Single	4 (13.8%)	3 (12.0%)	5 (19.2%)	12 (15.0%)		
Married	23 (79.3%)	19 (76.0%)	15 (57.7%)	57 (71.3%)		
Separation	1 (3.4%)	1 (4.0%)	1 (3.8%)	3 (3.8%)		
Divorced	0 (0.0%)	1 (4.0%)	4 (15.4%)	5 (6.3%)		
Widowed	1 (3.4%)	1 (4.0%)	1 (3.8%)	3 (3.8%)		
Education					11.041	.199
Below high school	3 (10.3%)	1 (4.0%)	6 (23.0%)	10 (12.5%)		
High school	6 (20.7%)	9 (36.0%)	7 (26.9%)	22 (27.5%)		
College and higher	20 (68.9%)	15 (60.0%)	13 (50.0%)	48 (60.0%)		
Survival period					12.402	.015
Within 5 years	25 (86.2%)	14 (56.0%)	17 (65.4%)	56 (70.0%)		
5-10 years	2 (6.9%)	11 (44.0%)	6 (23.1%)	19 (23.8%)		
>10 years	2 (6.9%)	0 (0.0%)	3 (11.5%)	5 (6.3%)		
Cancer type					4.149	.940
Colorectal cancer	2 (6.9%)	2 (8.0%)	3 (11.5%)	7 (8.8%)		
Lung cancer	1 (3.4%)	1 (4.0%)	1 (3.8%)	3 (3.8%)		
Malignant lymphoma	1 (3.4%)	3 (8.0%)	0 (0.0%)	3 (3.8%)		
Breast cancer	18 (62.1%)	16 (64.0%)	18 (69.2%)	52 (65.0%)		
Gynecological cancer	2 (6.9%)	2 (8.0%)	2 (7.7%)	6 (7.5%)		
Other types of cancer[a]	5 (17.2%)	2 (8.0%)	2 (7.7%)	9 (11.3%)		
Cancer staging				5.097		0.531
None stage[b]	1 (3.4%)	1 (4.0%)	1 (3.8%)	3 (3.7%)		
I	7 (24.1%)	11 (44.0%)	11 (42.3%)	29 (36.3%)		
II	15 (51.7%)	7 (28.0%)	7 (26.9%)	29 (36.3%)		
III	6 (20.7%)	6 (24.0%)	7 (26.9%)	19 (23.8%)		
Sense of fatigue					0.622	.733
No	12 (41.4%)	10 (40.0%)	13 (50.0%)	35 (43.8%)		
Yes	17 (58.6%)	15 (60.0%)	13 (50.0%)	45 (56.3%)		
Sense of anxiety					0.010	.995
No	22 (75.9%)	19 (76.0%)	20 (76.9%)	61 (76.3%)		
Yes	7 (24.1%)	6 (24.0%)	6 (23.1%)	19 (23.8%)		
Sense of depression					1.126	.569
No	22 (75.9%)	17 (68.0%)	21 (80.8%)	60 (75.0%)		
Yes	7 (24.1%)	8 (32.0%)	5 (19.2%)	20 (25.0%)		
Level of CRF at baseline					4.188	.381
None (score of 1-6)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		
Mild (score of 7-20)	5 (17.2%)	4 (16.0%)	9 (34.6%)	18 (22.5%)		
Moderate (score of 21-35)	21 (72.4%)	20 (80.0%)	15 (57.7%)	56 (70.0%)		
Severe (score of 36-50)	3 (10.3%)	1 (4.0%)	2 (7.7%)	6 (7.5%)		
Level of FOR at baseline					4.259	.642
None (score of 1-15)	1 (3.4%)	0 (0.0%)	0 (0.0%)	1 (1.3%)		
Mild (score of 16-35)	15 (51.7%)	11 (44.0%)	15 (57.7%)	41 (51.2%)		
Moderate (score of 36-55)	10 (34.5%)	13 (52.0%)	9 (34.6%)	32 (40.0%)		
Severe (score of 56-75)	3 (10.3%)	1 (4.0%)	2 (7.7%)	6 (7.5%)		

Abbreviations: E1, Qigong exercise group; E2, stress management group; CRF, cancer-related fatigue; FOR, fear of recurrence.
[a]Other types of cancer including gastric cancer, liver cancer, leukemia, nasopharyngeal carcinoma, and peritoneal mesothelioma.
[b]None stage including leukemia and peritoneal mesothelioma.

Table 3. The Paired Sample *t* Test and 1-Way ANOVA of 3 Groups (N = 80).

| | Improvement Effects of Single Interventions[a] | | | | | | | | | Between-Group Effects[b] | | | |
| | T1 vs T0 | | | T2 vs T0 | | | T2 vsT1 | | | T1-T0 | | T2-T0 | |
Variables	Mean (SD)	t	P	Mean (SD)	t	P	Mean (SD)	t	P	F	P	F	P
CRF										1.850	.164	1.416	.249
E1	−0.213 (0.499)	−2.307**	.029	−0.213 (0.550)	−2.093**	.046	0.000 (0.376)	0.000	1.000				
E2	−0.228 (0.514)	−2.216**	.036	−0.212 (0.506)	−2.095**	.047	0.016 (0.484)	0.165	.870				
Control	0.026 (0.602)	0.228	.822	0.015 (0.640)	0.122	.903	−0.011 (0.554)	−0.106	.916				
FOR										0.957	.389	0.750	.476
E1	−0.147 (0.687)	−1.153	.259	−0.211 (0.751)	−1.516	.141	−0.064 (0.437)	−0.793	.453				
E2	−0.173 (0.495)	−1.750	.093	−0.090 (0.619)	−0.732	.471	0.082 (0.422)	0.979	.337				
Control	0.028 (0.493)	0.292	.773	−0.007 (0.436)	−0.090	.929	−0.035 (0.439)	−0.417	.680				
QOL										1.092	.341	0.116	.890
E1	0.168 (0.587)	1.545	.134	0.026 (0.674)	0.212	.834	−0.141 (0.476)	−1.603	.120				
E2	0.090 (0.386)	1.173	.252	0.078 (0.370)	1.057	.301	−0.012 (0.337)	−0.182	.857				
Control	−0.017 (0.377)	−0.240	.813	0.011 (0.431)	0.140	.890	0.029 (0.284)	0.529	.601				
SDNN										9.332***	<.001	0.272	.763
E1	5.267 (5.657)	5.014***	<.001	1.178 (8.217)	0.772	.446	−4.088 (10.036)	−2.194**	.037				
E2	8.390 (5.274)	7.954***	<.001	2.369 (11.085)	1.069	.296	−6.021 (10.922)	−2.756**	.011				
Control	−0.881 (11.230)	−0.400	.692	0.140 (12.851)	0.056	.956	1.021 (6.737)	0.773	.447				
TP										7.307**	.001	2.129	.126
E1	203.008 (317.483)	3.443**	.002	47.782 (252.675)	1.018	.317	−155.225 (403.743)	−2.070**	.048				
E2	255.459 (259.103)	4.930***	<.001	55.154 (369.998)	0.745	.463	−200.304 (380.110)	−2.635**	.015				
Control	−72.903 (404.670)	−0.919	.367	−9.673 (479.527)	−0.103	.919	63.230 (237.924)	1.355	.188				
HF										0.943	.394	0.280	.756
E1	35.358 (59.786)	3.185**	.004	2.733 (77.064)	0.191	.850	−32.625 (89.502)	−1.963	.060				
E2	34.447 (77.034)	2.236**	.035	18.478 (144.497)	0.639	.529	−15.969 (119.591)	−0.668	.511				
Control	5.365 (124.007)	0.221	.827	29.711 (170.228)	0.890	.382	24.346 (106.030)	1.171	.253				

Abbreviations: ANOVA, analysis of variance; T0, baseline; T1, 12-weeks postintervention; T2, 3-month follow-up; CRF, cancer-related fatigue; E1, Qigong exercise group; E2, stress management group; FOR, fear of recurrence; QOL, quality of life; SDNN, standard deviation of normal R-R intervals, the index of overall autonomic nervous system activity; TP, total power, the index of overall activity heart rate variability; HF, high frequency, the index of parasympathetic nerve activity.
[a]Paired sample *t* test.
[b]One-way ANOVA.
**$P < .01$, ***$P < .001$ (2-tailed test).

Discussion

The results of this study show that the participants suffered from CRF (100%) and that 77.5% of them experienced moderate to severe fatigue. These findings suggest that the severity of CRF has been underestimated. Cancer survivors are often unaware of this condition; thus, its severity can be overlooked, resulting in delayed treatment. Our findings are consistent with those reported in related studies.[5,39]

Moreover, 98.7% of the participants displayed emotional distress symptoms due to FOR. Among these participants, 47.5% experienced moderate to severe fear, and 7.5% experienced severe fear. These findings are consistent with the results of related studies in which it was reported that 49% and 7% of cancer survivors suffered from moderate to severe and severe emotional distress, respectively.[4] A previous study reported that approximately 50% of cancer survivors experienced a lack of psychological support and care and urgently needed the support provided by social groups and activities.[7] Therefore, active participation by the medical staff in providing care and intervention support is critical.

Regarding CRF, QE and SM yielded statistically significant improvements at T1 and T2. QE restores mind-body balance by utilizing breathing exercises, repeated physical movements, and meditation. Symptoms of fatigue can be effectively alleviated, and the improvements can be maintained for a minimum of 3 months.[40] Intervention can be achieved by psychological education focused on emotional support, response strategies, and relaxation skills. Moreover, cognitive behaviors were reconstructed, which can actively relieve fatigue and emotional distress and improve problem-solving skills to promote self-efficacy and goal achievement.[28] These findings are consistent with the results obtained in our study.

Regarding FOR, a nonsignificant trend toward improvement was noted, but the scores were decreased at T1 and T2, indicating that emotional distress was slightly decreased. Cancer-related emotional distress is different from the distress experienced by healthy individuals. Such distress increases as the cancer survivor ages, as the disease progresses, or as new health issues develop. Moreover, the symptoms of distress can be persistent.[41] Symptoms tend to

Table 4. Time Effects of 3 Groups From AR1 Model of GEE Analysis (N = 80).

DV	IV	Estimate β	SE	Wald χ^2	P
CRF	Intercept	2.402	0.138	303.075***	<.001
	E1 vs control group	0.173	0.182	0.903	.342
	E2 vs control group	0.259	0.161	2.575	.109
	T1-T0	−0.140	0.060	5.344*	.021
	T2-T0	−0.139	0.635	4.777*	.029
FOR	Intercept	2.422	0.143	286.048***	<.001
	E1 vs control group	−0.094	0.185	0.258	.611
	E2 vs control group	0.119	0.196	0.364	.546
	T1-T0	−0.098	0.063	2.393	.122
	T2-T0	−0.108	0.068	2.439	.118
QOL	Intercept	3.953	0.125	997.134***	<.001
	E1 vs control group	−0.014	0.153	0.008	.928
	E2 vs control group	−0.062	0.156	0.158	.691
	T1-T0	0.084	0.052	2.595	.107
	T2-T0	0.038	0.056	0.448	.503
SDNN	Intercept	29.883	2.104	201.597***	<.001
	E1 vs control group	−4.446	2.765	2.585	.108
	E2 vs control group	−3.897	2.393	2.651	.103
	T1-T0	4.245	0.956	19.682***	<.001
	T2-T0	1.213	1.188	1.043	.307
TP	Intercept	492.471	72.249	46.462***	<.001
	E1 vs control group	−105.858	91.606	1.335	.248
	E2 vs control group	−98.154	78.120	1.579	.209
	T1-T0	129.728	39.815	10.616**	.001
	T2-T0	31.413	41.245	0.580	.446
HF	Intercept	104.976	20.797	25.479***	<.001
	E1 vs control group	−37.619	26.734	1.980	.159
	E2 vs control group	−19.075	27.803	0.471	.493
	T1-T0	25.326	10.018	6.391*	.011
	T2-T0	16.421	14.800	1.231	.267

Abbreviations: AR, autoregressive; GEE, generalized estimating equation; DV, dependent variable; IV, independent variable; SE, standard error; CRF, cancer-related fatigue; E1, Qigong exercise group; E2, stress management group; T0, baseline; T1, 12-week postintervention; T2, 3-month follow-up; FOR, fear of recurrence; QOL, quality of life; SDNN, standard deviation of normal R-R intervals, the index of overall autonomic nervous system activity; TP, total power, the index of overall activity heart rate variability; HF, high frequency, the index of parasympathetic nerve activity.
*$P < .05$, **$P < .01$, ***$P < .001$ (2-tailed test).

be more severe among females, individuals with lower socioeconomic status, and younger individuals.[7,42] Emotional distress has not been correlated with cancer prognosis, survival time, or cancer type. Correlated factors include the level of education received, whether recurrence or metastasis is experienced, and satisfaction with social support.[43] Cancer survivors realize the uncertainties in disease progress, health, and QOL. As found in our study, FOR does not decrease with longer survival time or with longer interventions. These findings are consistent with the results of related studies.[7,43] Therefore, continuous guidance on physical and psychological activities, nutrition management education, and periodic care should be provided. The fact that 87.5% of the participants in our study were female, a

population in which FOR is relatively more severe, might explain the diminished and insignificant intervention effects observed.

Regarding QOL, a nonsignificant trend toward improvement was noted, but the scores were increased at T1 and T2, indicating that QOL was slightly improved. Due to the severe impact of the disease on physical, emotional, and social functions, the QOL of cancer survivors decreases over time. Moreover, the decrease in QOL is more apparent among patients less than 50 years of age. Therefore, long-term care and interventions are necessary.[44] Approximately one third of the participants in our study were less than 50 years of age; this could be the main factor contributing to the insignificant effect of interventions on QOL.

Qigong and SM interventions yielded significant differences in HRV at T1 versus T2. They both resulted in improvements in SDNN and TP and also induced parasympathetic nervous system activation (HF). These intervention activities allow the mind-body to enter a relaxed state and promote the regulation of ANS function, resulting in stabilized emotions. Monitoring of mental and physical states through HRV reveals the benefits and effects of Qigong and SM on physical and psychological health in real time. These results are supported by related studies.[11,20,21,29,45,46]

The results of our study indicated that QE and SM both enhance the physical and psychological functions of cancer survivors. Furthermore, these activities relieve fatigue and ANS functional disorders.

Thus, when facing the uncertainty of cancer progression, patients can respond with a more stable mental status, a positive attitude, and increased confidence. Adjustments in diet and nutritional supplements are also indispensable to cancer survivors. Elimination of bad dietary habits and improvement in nutrition can allow the rapid restoration of physical functions and enhance immunity. Furthermore, facing disease and life with a positive attitude can improve symptoms and physical and mental energy levels.

This study has some limitations. Regarding effects over time, the effects during the follow-up phase (T2) were not as significant as the immediate effects at T1; however, the improvements were steadily maintained. Although demonstration DVDs and CDs were provided to the participants to encourage home practice, lack of persistence can result from lack of supervision and peer encouragement. We suggest that cancer survivors actively participate in long-term physical and psychological rehabilitation activities. Continuous and periodic involvement in practices led by professional coaches at a minimum frequency of once a week is recommended. Long-term educational resources and care should be provided to maintain long-term improvements. These suggestions are provided herein as a reference for clinical practice. Moreover, significant differences between groups were not observed. Such results may be attributed to the different nature of the interventions; QE emphasizes training in physical strength, whereas SM focuses on mental support. These interventions both yielded improvements. Hence, care should be taken to cultivate both mental and physical health, as they complement each other. In future studies, a crossover design is recommended to permit accurate evaluation of the significant effects of the interventions. Moreover, such a design will allow the survivors to receive both physical and psychological support, as cancer patients can benefit from both activities.

Conclusion

In our study, questionnaires and HRV were employed to evaluate the condition of cancer survivors during recovery. The results suggest that QE and SM affect HRV in addition to CRF, which is an interesting finding on its own. Although the questionnaires employed were reliable and effective, the responses were based on subjective opinions and personal feelings and may not truly reflect the mental and physical health of cancer survivors. In contrast, HRV provides effective monitoring of heart and lung function and the status of ANS balance. Because the progress of cancer patients can be monitored easily and rapidly with HRV, this approach can serve as an indicator for evaluating the mind-body state after treatment and can assist medical providers in providing comprehensive care. Providing scientific support for the effectiveness of HRV is the focus of our future study.

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