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Original Article

Positive influence of managing cancer and living meaningfully (CALM) on fear of cancer recurrence in breast cancer survivors

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Abstract: To evaluate the effectiveness and feasibility of managing cancer and living meaningfully (CALM), an intervention used to reduce the fear of cancer recurrence (FCR) in breast cancer survivors and improve their quality of life (QoL). A total of 103 breast cancer survivors were enrolled. Participants were randomly assigned to the CALM group or the care as usual (CAU) group. The participants completed a survey at baseline (T0) and after two (T1), four (T2), and six (T3) intervention sessions. The patients were assessed using the Cancer Worry Scale (CWS), Psychological Distress Thermometer (DT), Functional Assessment of Cancer Therapy-Breast (FACT-B) and Hospital Anxiety and Depression Scale (HADS). After the intervention, the CALM group showed a significant decrease in levels of FCR, distress, anxiety, and depression (χ^2=154.353, χ^2=130.292, χ^2=148.879, and χ^2=78.681; P<0.001, 0.001, 0.001, and 0.001, respectively) and an increased QoL (χ^2=122.822, P<0.001). Compared with the CAU group, the CALM group showed significant differences in FCR, distress, QoL, anxiety and depression (F=292.431, F=344.156, F=11.115, F=45.124, and F=16.155; P<0.001, P<0.001, P=0.01, P<0.001, and P<0.001, respectively). Negative correlations were found between CWS and FACT-B scores in the CALM group (T0: r=-0.6345, P<0.001; T1: r=-0.4127, P=0.0017; T2: r=-0.2919, P=0.0306; and T3: r=-0.3188, P=0.0177) and in the CAU group (T0: r=-0.7714, P<0.0001; T1: r=-0.6549, P<0.0001; T2: r=-0.5060, P=0.0002; and T3: r=-0.3151, P=0.0291). Thus, the CALM intervention reduced FCR, distress, anxiety and depression in breast cancer survivors and improved QoL.

Keywords: Breast cancer, fear of cancer recurrence, CALM intervention, quality of life

Introduction

In 2020, breast cancer was the most common cancer in women, according to global cancer statistics [1]. In China, the number of new breast cancer cases increased from 0.3 million in 2015 to 0.42 million in 2020, making it the fourth most common kind of cancer in the country [2]. The treatments for breast cancer include chemotherapy, radiotherapy, endocrine therapy and targeted therapy. Immunotherapy is an effective treatment for various solid tumours [3], but breast cancer is not very sensitive to immunotherapy. Recently, Wenjie Shi et al. used machine learning and immunohistochemistry validation to verify that COL11A1 is a potential therapeutic target for breast cancer treatment and may be involved in tumour immune infiltration. High expression of this protein is closely related to poor prognosis for patients with breast cancer, highlighting an opportunity to administer immunotherapy to treat breast cancer [4]. With advancements in drugs and programs used to treat breast cancer, the five-year survival rate is as high as 90% [5]. With the extension of survival time, increasing efforts have focused on improving patients' quality of life (QoL). Breast cancer survivors (BCSs) often experience psychosocial disturbance, which is an unpleasant emotional experience influenced by psychological, social and spiritual factors, mainly manifesting as fear of cancer recurrence (FCR), anxiety, depression, and psychological distress.

FCR is a common problem reported by cancer survivors and is defined as "fear, worry, or concern about the recurrence or progression of cancer" [6]. Previous studies have shown that FCR is the second most common problem reported by BCSs, with 22% to 99% reporting FCR [7-9]. Mild or transient FCR is normal and can stimulate appropriate healthy behaviour, while persistent and excessive FCR can heighten the risks of depression, impairment of daily function, and unnecessary health assessments, which have a negative impact on the QoL of survivors [10]. Studies have shown that even when the risk of recurrence is low, FCR usually does not decrease over time [11]. FCR is an important and distressing problem affecting many cancer survivors, and there is clear evidence that cancer survivors with moderate to severe FCR experience greater psychological distress and may incur additional medical costs [12]. Many BCSs manage FCR through poor adaptability, excessive vigilance, or avoidant coping [13, 14]. However, an overly vigilant coping style may lead to patients pursuing daily breast self-examinations or unnecessary medical examinations. In contrast, patients with an avoidant coping style refuse to face the fact that they have had cancer by trying to ignore it [15]. Although escape reduces stress in the short term, this coping behaviour often fails in the long term, and thoughts of death become increasingly intrusive. Several large studies have found that 21-40% of cancer survivors report needing help to address FCR [12, 16]. Considering the negative impact of FCR on the physical and psychological health of patients, an effective intervention to alleviate FCR is urgently needed.

Other psychological disturbances, such as anxiety, depression and psychological distress, were also reported to reduce the QoL of patients [17-19]. These disturbances, in turn, are associated with worse medical compliance and increased barriers to cancer care, including a lack of understanding of treatment recommendations and adverse reactions to treatment, and may even increase mortality [20, 21]. Therefore, the psychological symptoms experienced by cancer patients have attracted increasing attention. The numbers of psychological and drug interventions are increasing, and the National Comprehensive Cancer Network (NCCN) has provided new management guidelines for the psychological problems of cancer patients, such as cognitive behavioural therapy, supportive psychotherapy and family and couples therapy [22]. However, drug therapy involves the risks of dependence and side effects, such as insomnia and gastrointestinal discomfort; therefore, psychological interventions seem to be more acceptable to patients.

The CALM intervention is one of the psychotherapy methods proposed by Gary Rodin to decrease depression and death anxiety and to improve mental well-being in patients with advanced cancer. It is a new, brief, and patient-tailored supportive psychotherapeutic intervention and is designed to help cancer patients live a meaningful life and reduce psychological suffering [23, 24]. CALM focuses on the following four areas: (1) managing symptoms and communicating with health care providers, (2) changing oneself and close relationships, (3) seeking mental health and a meaningful life, and (4) facing death and the future bravely. These areas have been identified as areas of common concern and sources of suffering for people with advanced cancer [25].

In trials with advanced cancer survivors, studies have shown that CALM is an effective psychological intervention that can reduce depression, death-related anxiety, and mental health problems and improve attachment security [26, 27]. Mindfulness-based cognitive therapy, blended cognitive behaviour therapy, and the ConquerFear intervention have been confirmed to reduce FCR severity in cancer survivors [28-30]. However, there are few reports on the efficacy of the CALM intervention on FCR in BCSs; thus, we conducted a randomized controlled trial to evaluate the effectiveness and feasibility of this intervention. The primary outcomes were the severity of FCR and its correlation with QoL, while the secondary outcomes included psychological distress, QoL, anxiety, and depression.

Materials and methods

Test design and procedures

BCSs were identified by prescreening test results, and eligible patients were recruited in oncology wards, where the oncologists introduced the contents of the experiment to the patients; interested patients signed informed

consent forms. The researchers assessed the cognitive function, readiness, and ability to engage of participants and collected baseline measurements. Patients with Cancer Worry Scale (CWS) scores ≥14 were randomly assigned to the CALM intervention group or the CAU group. Participants in the CALM group underwent six CALM sessions. Participants in the CAU group received only usual care, which included routine oncology treatment and follow-up. Evaluations were conducted at baseline and after 2, 4, and 6 intervention sessions; at these timepoints, worry, distress, QoL, anxiety and depression were assessed. The study was approved by the Research Ethics Committee of the Affiliated Second Hospital of Anhui Medical University (approval no. 2012-088) and conformed to the ethical principles of the Declaration of Helsinki.

Participants

In total, 103 breast cancer patients with CWS scores ≥14 from the Department of Oncology of the Affiliated Second Hospital of Anhui Medical University were enrolled in this study from January 2022 to August 2022. The patients were divided into 2 groups. The CALM intervention group was composed of 55 BCSs, and the CAU group included 48 BCSs.

The inclusion criteria for patients were as follows: (1) were pathologically diagnosed with breast cancer with a life expectancy of more than 6 months and had received no prior psychological treatment; (2) had a CWS score ≥14; (3) had a Karnofsky Performance Status (KPS) score ≥80; (4) were at least 18 years old; and (5) had no hearing, vision, language or other functional impairments (i.e., were able to provide written informed consent and independently complete the questionnaire).

The exclusion criteria were as follows: (1) received psychological or psychiatric treatment, (2) had a severe mental illness or cognitive impairment, or (3) had advanced cachexia.

Intervention

The design of the experiment was evaluated by experts in the field, including two psychologists and an oncologist, to ensure the feasibility, practicability and scientificity of the experiment. Participants in the CALM group underwent six CALM sessions over a period of four to six months. Each session lasted 45 to 60 minutes, and the first three treatments were completed within the first month. Then, subjects received a session once a month for 3 months. The CALM intervention is a brief, personalized, mechanized psychotherapy intervention addressing the following four areas: managing symptoms and communicating with healthcare providers, changing oneself and close relationships, seeking mental health and a meaningful life, and facing death and the future bravely [25]. The time spent on each area and the order in which these areas were addressed were tailored to the needs of the patient. CALM sessions were conducted in a separate room with comfortable music playing in the background to ensure patients' privacy and effective communication between the psychologist and participants. The sessions involved communicating with patients, providing accessible breast cancer-related knowledge, changing patients' incorrect beliefs regarding breast cancer, alleviating anxiety, increasing patient confidence in their treatment, helping patients to achieve physical and mental relaxation, encouraging patients to communicate with their relatives and friends, and facilitating integration into society. To ensure the therapeutic integrity of the intervention team, the therapists were monitored weekly and instructed to submit case reports and record their conversations with patients in written reports. In addition, examiners assessed the overall quality of the intervention and discussed it with each therapist to improve their capacity.

Assessments

Fear of cancer recurrence: The CWS was used to evaluate the severity of FCR, and the correlation between CWS scores and QoL was analysed. The CWS is an effective tool for detecting FCR in BCSs, and all items are scored on a four-point scale ranging from 1 (never) to 4 (almost always). The scale has good psychometric properties (α=0.87). The total score ranges from 8 to 32, with higher scores indicating more severe FCR [31]. Participants with CWS scores ≥14 were classified as having a severe FCR and were eligible to participate [32]; CWS scores were also used as a primary outcome measure.

Quality of life: QoL was assessed with the Functional Assessment of Cancer Therapy-

Breast (FACT-B), which is divided into 5 subscales and 36 items, namely, physical well-being (7 items), social/family well-being (7 items), emotional well-being (6 items), functional well-being (7 items) and a specific breast-cancer subscale (9 items). The scores on each item, each subscale and the total scale can be calculated. Each item is rated on a five-point scale from 0 (not at all) to 4 (very), with an overall score ranging from 0 to 144, with higher scores indicating better QoL.

Distress: Distress was measured with the Psychological Distress Thermometer (DT). The DT involves a graphic of a typical thermometer upon which subjects indicate their level of distress. Scores range from 0 to 10, with 0 indicating no distress and 10 indicating extreme distress. The higher the score is, the more severe the distress.

Anxiety and depression: Anxiety and depression were measured with the Hospital Anxiety and Depression Scale (HADS), which includes two subscales of anxiety (HADS-A) and depression (HADS-D). Each item is rated on a scale from 0 to 3, and the total score of each subscale ranges from 0 to 21. The higher the score is, the more severe the symptoms. Scores on each subscale are categorized as follows: asymptomatic (1-7 points), borderline (8-10 points), or positive (11-21 points; i.e., presence of depression or anxiety).

Statistical analysis

All statistical analyses were performed using SPSS version 26 and were expressed as the mean ± standard deviation. All statistical tests were two tailed, and findings were considered statistically significant at $P<0.05$. The Kolmogorov-Smirnov test was used to determine whether the data conformed to a normal distribution. Baseline differences in demographic and medical characteristics between groups determined by an independent-sample t test or chi-square test, as appropriate. Independent-sample t tests were used to compare the questionnaire scores at baseline (T0) between the CALM and CAU groups. Scores before and after the 2, 4, and 6 intervention sessions were analysed with the Friedman test. Repeated-measures analysis of variance (ANOVA) was used to compare the scores of the CALM group and the CAU group over time. Pearson correlation analysis was used to examine the relationship between CWS scores and QoL.

Results

Baseline demographic and clinical data

Figure 1 shows the research flowchart. A total of 150 BCSs completed the CWS; of these, 24 were not qualified to participate after application of the inclusion and exclusion criteria (e.g., total score on the CWS<14), resulting in 126 included participants. These participants were equally allocated to the CALM group and CAU group (n=63 in each group), but some participants were lost to follow-up. Thus, data from 55 participants in the CALM group and 48 participants in the CAU group were analysed.

Table 1 shows the clinical characteristics of participants according to group. Comparison of the CALM and CAU groups revealed no significant differences in demographic characteristics, such as age ($t=0.911$, $P=0.365$), education level ($\chi^2=4.407$, $P=0.221$), and presence or absence of a partner ($\chi^2=0.149$, $P=0.700$), or clinical characteristics, including cancer stage ($\chi^2=4.695$, $P=0.196$), pathological type ($\chi^2=1.236$, $P=0.539$), treatment method ($\chi^2=0.491$, $P=0.974$), and KPS ($\chi^2=1.572$, $P=0.210$), at baseline.

Postintervention scores in the CALM and CAU groups

Scores on the CWS, DT, FACT-B, HADS-A, and HADS-D before and after the intervention in the CALM and CAU groups are shown in **Tables 2** and **3**. After the intervention, the CALM group showed significant decreases in the levels of FCR, distress, anxiety, and depression ($\chi^2=154.353$, $\chi^2=130.292$, $\chi^2=148.879$, and $\chi^2=78.681$; $P<0.001$, 0.001, 0.001, and 0.001, respectively) and a higher QoL ($\chi^2=122.822$, $P<0.001$). In contrast, the CAU group showed significant increases in CWS, DT, HADS-A and HADS-D scores ($\chi^2=102.290$, $\chi^2=132.918$, $\chi^2=118.705$, and $\chi^2=65.155$; $P<0.001$, 0.001, 0.001, and 0.001, respectively) and a lower QoL ($\chi^2=133.411$, $P<0.001$).

Comparison of the intervention effects

There were no significant differences between the CALM group and the CAU group in each

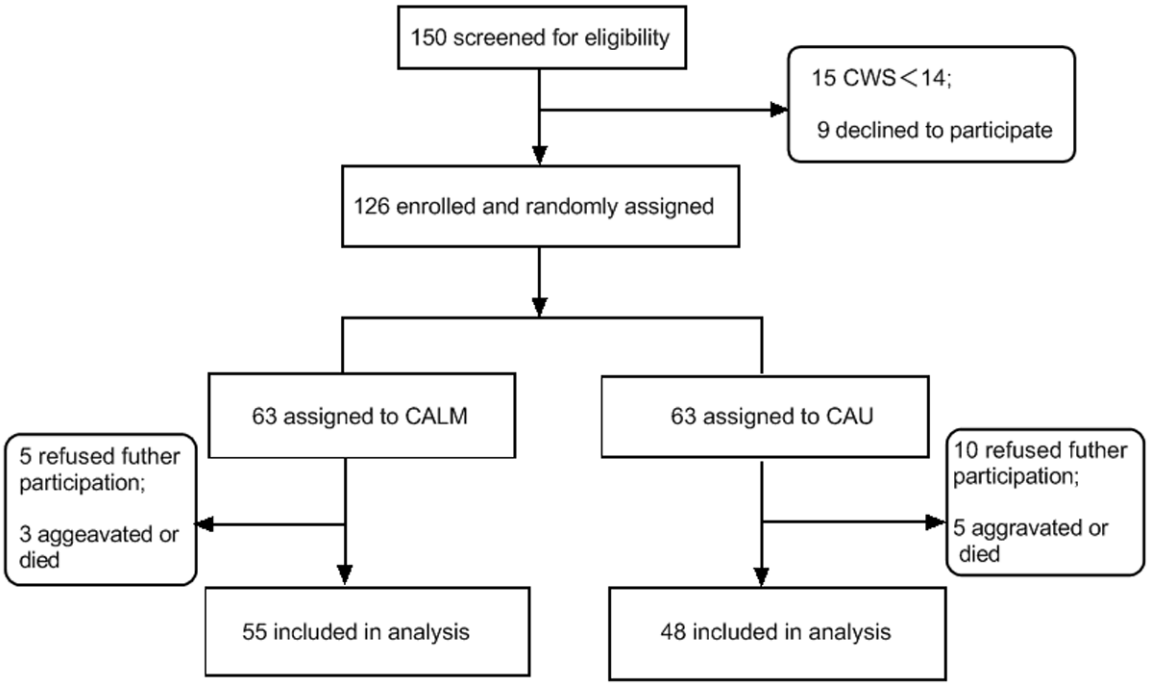

Figure 1. Research flowchart.

Table 1. The demographic characteristics and clinical information of the patients

Characteristics	CALM (n=55)	CAU (n=48)	t/χ	P
Age (years), mean ± SD	52.75±7.799	51.15±10	0.911	0.365
Education, n (%)			4.407	0.221
Illiteracy	27 (49.1)	19 (39.6)		
Primary school	21 (38.2)	15 (31.2)		
Middle school	6 (10.9)	11 (22.9)		
University and above	1 (1.8)	3 (6.3)		
Tumor stage, n (%)			4.695	0.196
I	3 (5.5)	8 (16.7)		
II	13 (23.6)	12 (25.0)		
III	7 (12.7)	8 (16.7)		
IV	32 (58.2)	20 (41.6)		
Pathological type, n (%)			1.236	0.539
Early invasive carcinoma	4 (7.3)	6 (12.5)		
Special type of cancer	3 (5.4)	4 (8.3)		
Non-specific type of cancer	48 (87.3)	38 (79.2)		
Previous treatment, n (%)			0.491	0.974
Surgery + chemotherary	23 (41.8)	21 (43.8)		
Chemotherary + radiotherarpy	5 (10.0)	3 (6.2)		
Chemotherary + endocrinothrapy	7 (12.7)	7 (14.6)		
Chemotherary + targeted therapy	13 (23.6)	12 (25.0)		
Chemotherary	7 (12.7)	5 (10.4)		
Partner status, n (%)			0.149	0.700
Yes	43 (78.2)	39 (81.2)		
No	12 (21.8)	9 (18.8)		
KPS, n (%)			1.572	0.210
80	30 (54.5)	32 (66.7)		
90	25 (45.5)	16 (33.3)		

Abbreviations: SD, standard deviation; KPS, Karnofsky performance status; CALM, Managing Cancer and Living Meaningfully; CAU, care as usual. Data are presented as mean ± SD.

Table 2. Separate comparison of symptoms over the course of treatment in the CALM group

Item (mean ± SD)	CALM (n=55)				χ^2	P
	T0[a]	T1[a]	T2[a]	T3[a]		
CWS	17.65±1.65	15.95±1.99	12.15±2.24	8.24±1.89	154.353	<0.001
DT	4.35±0.73	3.71±0.63	2.98±0.73	1.93±0.63	130.292	<0.001
FACT-B	66.31±9.25	69.42±8.41	72.62±7.90	77.55±6.10	122.822	<0.001
HADS-A	9.53±2.58	8.75±2.60	7.10±2.52	4.91±2.14	148.879	<0.001
HADS-D	10.24±3.08	9.29±2.48	8.05±2.05	7.11±1.87	78.681	<0.001

Abbreviations: CALM, Managing Cancer and Living Meaningfully; SD, standard deviation; CWS, The Cancer Worry Scale; DT, Distress Thermometer; FACT-B, Functional Assessment of Cancer Therapy-Breast cancer patient; HADS-A, the Hospital anxiety and Depression scale-anxiety; HADS-D, the Hospital anxiety and Depression scale-depression; T0[a], before CALM treatment; T1[a], after 2 CALM sessions; T2[a], after 4 CALM sessions; T3[a], after 6 CALM sessions.

Table 3. Separate comparison of symptoms over the course of treatment in the CAU group

Item (mean ± SD)	CAU (n=48)				χ^2	P
	T0[b]	T1[b]	T2[b]	T3[b]		
CWS	17.27±2.92	18.77±2.47	20.35±2.35	22.00±2.50	102.29	<0.001
DT	4.04±0.90	4.85±0.85	6.02±0.89	7.15±0.97	132.918	<0.001
FACT-B	70.14±14.31	67.23±13.97	63.63±13.64	57.10±12.20	133.411	<0.001
HADS-A	8.83±2.85	10.29±2.77	11.56±2.95	13.10±3.19	118.705	<0.001
HADS-D	9.15±2.81	10.52±2.72	11.15±2.63	11.29±3.16	65.155	<0.001

Abbreviations: CAU, care as usual; SD, standard deviation; CWS, The Cancer Worry Scale; DT, Distress Thermometer; FACT-B, Functional Assessment of Cancer Therapy-Breast cancer patient; HADS-A, the Hospital anxiety and Depression scale-anxiety; HADS-D, the Hospital anxiety and Depression scale-depression; T0[b], before CAU treatment; T1[b], after 2 CAU sessions; T2[b], after 4 CAU sessions; T3[b], after 6 CAU sessions.

Table 4. Comparison of symptoms between the CALM group and the CAU group

Item (mean ± SD)	CALM (n=55)				CAU (n=48)				F	P
	T0[a]	T1[a]	T2[a]	T3[a]	T0[b]	T1[b]	T2[b]	T3[b]		
CWS	17.65±1.65	15.95±1.99	12.15±2.24	8.24±1.89	17.27±2.92	18.77±2.47	20.35±2.35	22.00±2.50	292.431	<0.001
DT	4.35±0.73	3.71±0.63	2.98±0.73	1.93±0.63	4.04±0.90	4.85±0.85	6.02±0.89	7.15±0.97	344.156	<0.001
FACT-B	66.31±9.25	69.42±8.41	72.62±7.90	77.55±6.10	70.14±14.31	67.23±13.97	63.63±13.64	57.10±12.20	11.115	0.01
HADS-A	9.53±2.58	8.75±2.60	7.10±2.52	4.91±2.14	8.83±2.85	10.29±2.77	11.56±2.95	13.10±3.19	45.124	<0.001
HADS-D	10.24±3.08	9.29±2.48	8.05±2.05	7.11±1.87	9.15±2.81	10.52±2.72	11.15±2.63	11.29±3.16	16.155	<0.001

Abbreviations: CALM, Managing Cancer and Living Meaningfully; CAU, care as usual; SD, standard deviation; CWS, The Cancer Worry Scale; DT, Distress Thermometer; FACT-B, Functional Assessment of Cancer Therapy-Breast cancer patient; HADS-A, the Hospital anxiety and Depression scale-anxiety; HADS-D, the Hospital anxiety and Depression scale-depression; T0[a], before CALM treatment; T1[a], after 2 CALM sessions; T2[a], after 4 CALM sessions; T3[a], after 6 CALM sessions; T0[b], before CAU treatment; T1[b], after 2 CAU sessions; T2[b], after 4 CAU sessions; T3[b], after 6 CAU sessions.

scale score at T0 (CWS: t=0.806, P=0.423; DT: t=1.898, P=0.61; FACT-B: t=-1.581, P=0.118; HADS-A: t=1.296, P=0.198; and HADS-D: t=1.866, P=0.65). As shown in **Table 4**, compared with the CAU group, the CALM group showed significant differences in FCR, distress, QoL, anxiety and depression (F=292.431, F=344.156, F=11.115, F=45.124, and F=16.155; P<0.001, P<0.001, P=0.01, P<0.001, and P<0.001, respectively). As shown in **Figure 2**, the CWS, DT, HADS-A, and HADS-D scores tended to decline in the CALM group, while the FACT-B scores tended to increase. In contrast, in the CAU group, CWS, DT, HADS-A, and HADS-D scores showed an increasing trend, and FACT-B scores showed a decreasing trend.

Relationship between QoL and FCR in the CALM group and the CAU group

As shown in **Figures 3** and **4**, negative correlations were found between CWS and FACT-B scores at each timepoint in the CALM group (T0[a]: r=-0.6345, P<0.001; T1[a]: r=-0.4127, P=0.0017; T2[a]: r=-0.2919, P=0.0306; and T3[a]: r=-0.3188, P=0.0177) and in the CAU group

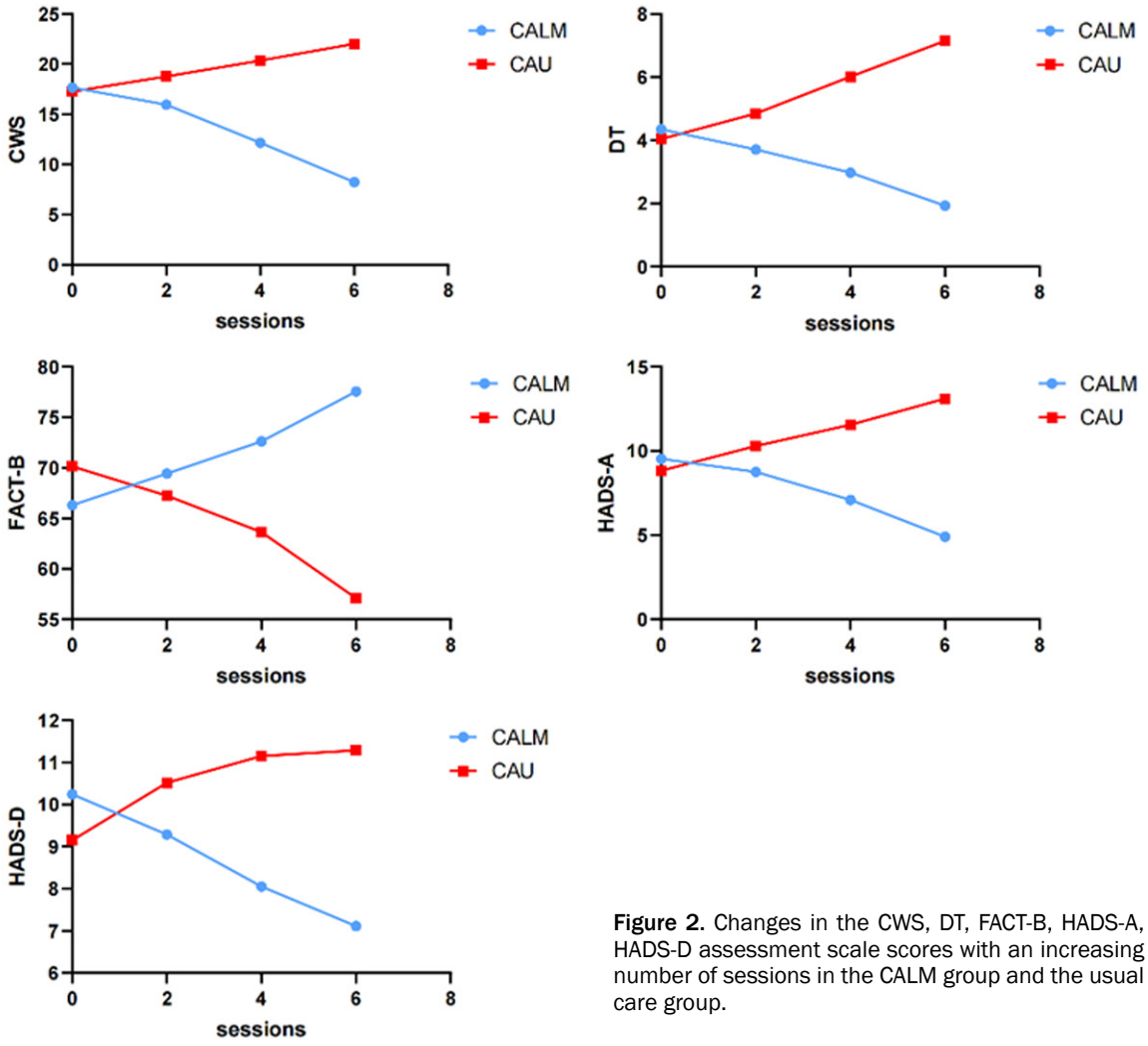

Figure 2. Changes in the CWS, DT, FACT-B, HADS-A, HADS-D assessment scale scores with an increasing number of sessions in the CALM group and the usual care group.

(T0[b]: r=-0.7714, P<0.0001; T1[b]: r=-0.6549, P<0.0001; T2[b]: r=-0.5060, P=0.0002; and T3[b]: r=-0.3151, P=0.0291). In other words, the more severe FCR was, the worse the QoL in BCSs.

Discussion

In this study, we aimed to investigate the effectiveness of the CALM intervention for reducing FCR in BCSs. We found that the CALM intervention significantly reduced the psychological distress experienced by BCSs, including FCR, distress, anxiety and depression, and improved their QoL. Finally, we found a negative correlation between FCR and QoL. Our study provides further evidence of the effectiveness of the CALM intervention in BCSs.

The mental health of patients with advanced cancer is inevitably challenged by physical pain and disability, the imminent threat of death, the need for support, dramatic changes in relationships, and the challenges of navigating a complex health care system and making life-or-death treatment decisions [33]. Many international organizations, such as the World Health Organization, the European Collaboration for Palliative Care Research and the International Society of Psychological Oncology [34], have emphasized the need for psychotherapy for patients with cancer. CALM, a kind of psychotherapy, is an effective treatment, with studies demonstrating improvements in depression, anxiety, mental health and attachment security [23, 26]. CALM was developed on the basis of empirical data and clinical observations as well as the theoretical bases of relationship theory, attachment theory and existential theory. It has the following characteristics: 1) applicability for patients with an

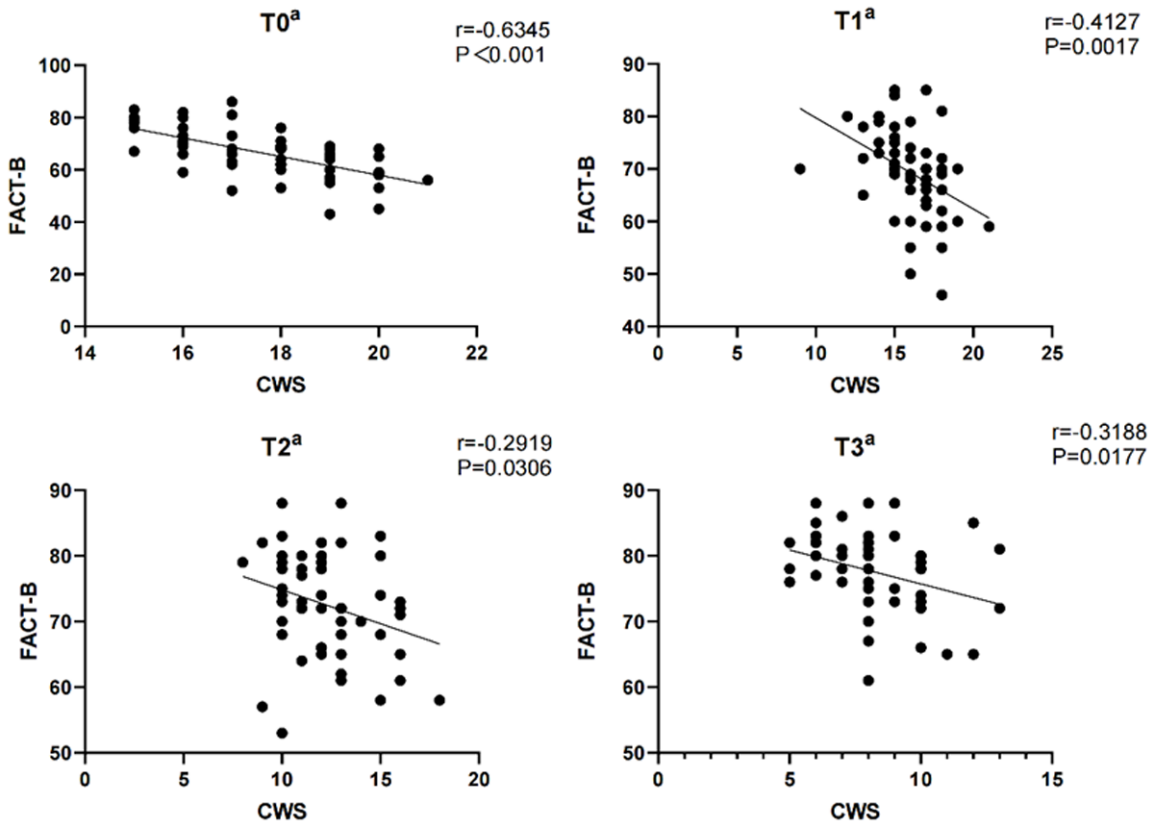

Figure 3. Relationships between QOL and FCR in the CALM group. Note: T0[a], Before CALM treatment; T1[a], After 2 CALM sessions; T2[a], After 4 CALM sessions; T3[a], After 6 CALM sessions.

expected prognosis of more than one year; 2) emphasis on personalization; 3) focus on four empirically identified, broad areas of disease experience for advanced cancer; and 4) focus on the process of spiritualization and attachment security [26]. CALM is tailored to each patient, allowing variation in the number and timing of sessions according to the patient's needs and health status. CALM sessions include five interrelated themes according to survivor needs: 1) a safe place to deal with terminal cancer experiences, 2) ability to talk about death and dying, 3) help with managing the disease and navigating medical systems, 4) alleviation of tensions, and 5) being "seen as a whole person" within the healthcare system [24].

At the end of each session, patients are provided with the chance to speak freely and "dump" or "vent" their thoughts and feelings in a safe place. Finally, patients are provided with guidance for their specific problems. As part of the session, participants revealed that the CALM sessions were the only place where discussions about death and dying were encouraged and allowed. Talking about death during treatment helped patients to overcome their fear of bringing it up with loved ones, which was a vast relief for them and also facilitated subsequent conversations with family members. The CALM intervention also encouraged therapists to provide important nonspecific therapeutic characteristics, such as listening to patients nonjudgmentally and empathetically and supporting the process of reflection. After the intervention, participants were able to maintain communication with their therapist, and when they encountered unmanageable problems, they could return if necessary to ensure the integrity of continuous monitoring and treatment. This guarantee could reduce the related anxiety and loneliness and improve their mood. In turn, the therapists could better understand patients' thoughts and feelings and provide better support for future treatment. The benefit of the CALM intervention may be attributed to the fact that it provides BCSs with opportuni-

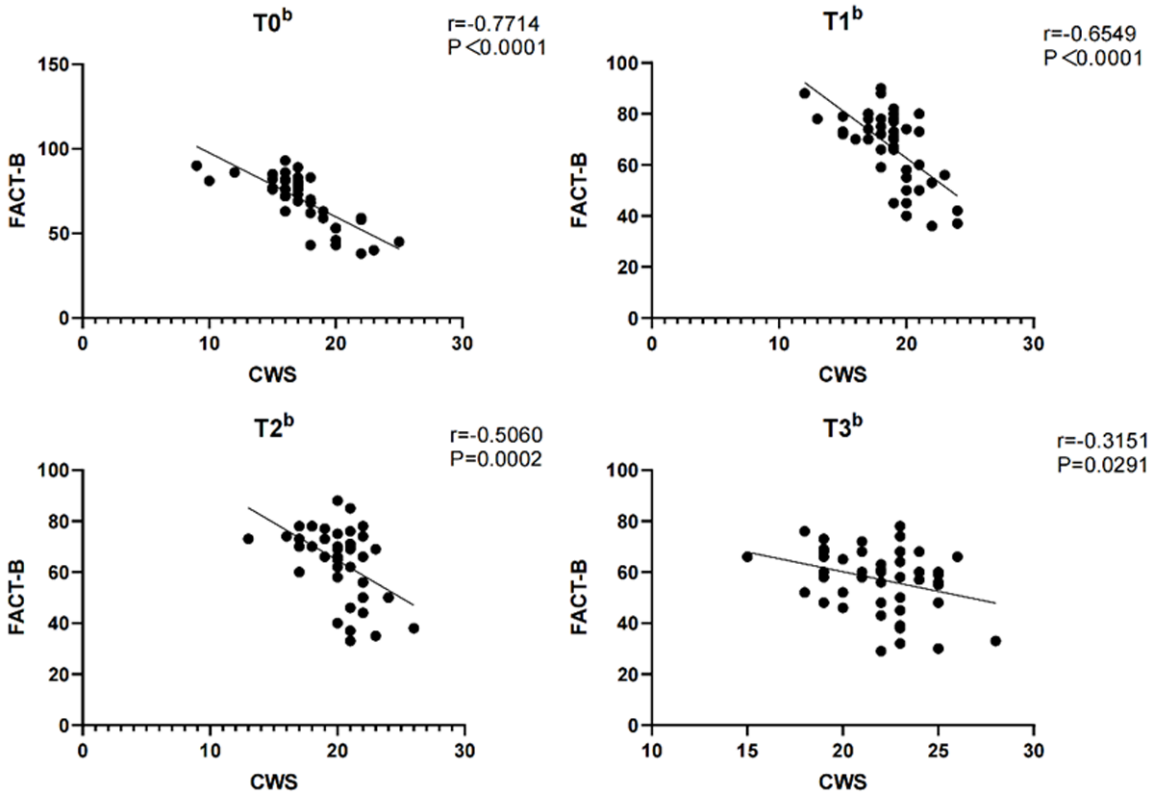

Figure 4. Relationships between QOL and FCR in the usual care group. Note: T0[b], Before CAU treatment; T1[b], After 2 CAU sessions; T2[b], After 4 CAU sessions; T3[b], After 6 CAU sessions.

ties for communication and reflection, helps them to solve practical problems and provides support to address the complex and painful problems caused by cancer.

FCR has a substantial impact on the lives of cancer survivors and their families. In this study, we found that the FCR of BCSs in the CALM group showed a decreasing trend, while the FCR of BCSs in the CAU group showed the opposite trend. A study of patients with early-stage breast cancer showed that 70% reported a clinical level of FCR, 25% said that FCR severely damaged their mood, and 19% reported that it significantly impaired their ability to make plans and set future goals [35]; thus, there is an urgent need to treat FCR. Yuan Yang et al. showed that different treatment modalities did not differ in FCR induced but that higher treatment intensity was significantly associated with increased FCR and that physical and cognitive impairments due to the side effects of treatment was an important cause of increased FCR [14, 36]. One possible reason is that the more intense the treatment is, the longer the treatment duration and the greater the side effects; furthermore, these symptoms may serve as a constant reminder of the disease and further increase FCR in patients. However, the CALM intervention does not cause any physical trauma or drug-related side effects and can be applied over a long time, helping to reduce cancer-related pain, relieve short-term and long-term anxiety and depression caused by postoperative chemotherapy, effectively reduce FCR, and improve the happiness and QoL of cancer patients [37]. Therefore, we speculate that the mechanism underlying the benefits of the CALM intervention in reducing FCR may be related to these factors. However, further study is needed to determine the exact mechanism of FCR reduction by the CALM intervention in BCSs.

Although FCR was the primary outcome in this study, our secondary outcomes were also highly important. We confirmed that the CALM intervention was effective for reducing distress, anxiety, and depression and improving QoL in BCSs.

Psychological distress is a multifaceted unpleasant experience that may have a negative impact on a patient's ability to cope with cancer symptoms and treatment. We found that the CALM intervention was effective in alleviating psychological distress in BCSs. During and even after cancer treatment, BCSs experience a variety of physical, psychological, social and mental problems associated with the disease and its treatment. Up to 50% of BCSs experience psychological distress [38]. According to a meta-analysis, psycho-oncologic interventions, including individual psychotherapy, group psychotherapy, psychoeducation, and relaxation training, have small-to-medium effects on psychological distress [39]. The study found that psychological distress is closely related to mood disorders (including stress, anxiety and depression) and can affect the QoL of patients [40]. Therefore, we speculate that psychological distress may lead to FCR and that the CALM intervention may improve FCR by decreasing psychological distress. We plan to explore the relationship between psychological distress and FCR in greater depth in the future.

A meta-analysis showed that the prevalence rates of depression and anxiety in BCSs were 32.2% and 41.9%, respectively [41, 42]. Depression and anxiety may affect the physiological function, treatment compliance, psychological function and QoL of BCSs and may be important factors that affect mortality [43]. The oncology literature suggests that increased levels of anxiety and depression in women with breast cancer predict poor QoL and overall health outcomes [44]. Our results confirm the effectiveness of CALM in reducing anxiety and depression in BCSs. Therefore, in daily clinical practice, we should promote the screening of depression and anxiety and familiarity with associated treatments; this knowledge can help health care providers and policymakers to design better and more effective cancer treatment and control strategies.

Consistent with previous studies, we found that the CALM intervention improved the QoL of patients and that QoL was negatively correlated with FCR [36]. The survival rate of breast cancer patients has increased in the past 20 years, leading to increasing scrutiny of long-term QoL. QoL in these patients may be affected by early menopause, infertility, negative psychosocial effects, and the risk of recurrence and actual recurrence of primary breast cancer [45-47]. Given these long-term psychological pressures, the proportion of BCSs with mental illnesses is higher than that of the general population [48]. We believe that this is closely related to the management of advanced cancer and can be improved through interventions. Therefore, it is necessary for oncologists to provide interventions to improve the mental health of patients while treating the disease to improve patients' QoL. Our study further emphasizes the need for interventions, such as CALM, to alleviate FCR in patients.

The limitations of this study include its single-centre nature and small sample size; thus, the results may not be generalizable to other patients. The participants were all women with breast cancer. It is believed that men and women deal with emotional problems in different ways; women are more willing to express their feelings than men and are more likely to seek and accept help. Therefore, it is unclear whether a similar effect of the CALM intervention would be observed in male cancer patients. Second, this study mainly focused on patients with severe FCR; it remains unclear whether the intensity of this intervention is applicable to patients with mild and moderate FCR. In addition, many statistical comparisons were made in this study to examine a variety of results; however, we did not adjust the significance level, which may have increased the chance of type I errors. Finally, we did not follow the participants over a long period and thus are unable to establish the long-term effectiveness of the CALM intervention.

Conclusion

The CALM intervention reduced FCR, distress, anxiety and depression in BCSs and improved their QoL. These results suggest that CALM is an effective psychological intervention to alleviate FCR, anxiety and depression in patients with breast cancer.

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Disclosure of conflict of interest

None.

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