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# Cognitive-Behavioral Therapy and Hypnosis Intervention on Anxiety, Depression, and Quality of Life in Patients with Breast Cancer Undergoing Chemotherapy: A Clinical Trial

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### Abstract

**Background:** Women with breast cancer undergo painful and distressing treatment procedures. Hypnotherapy and cognitive-behavioral therapy (CBT) could be considered as an effective therapy.

**Method:** In this clinical trial, 50 women aged 25 to 65 were assigned to three groups (CBT, hypnosis, and control groups). Eight one-hour treatment sessions were run for each of the hypnosis and CBT groups. We utilized The European Organization for Research and Treatment of Breast Cancer-specific Quality of Life (QoL), The European Organization for Research and Treatment of Cancer QoL questionnaires, and The Hospital Anxiety and Depression Scale for the evaluation of the QoL, anxiety, and depression at the beginning and end of the treatment, as well as six months post-treatment.

**Results:** The improvements in the stress, depression, and qoL amongst the three groups were significant, although these improvements in CBT group were more than those in hypnosis group, and in hypnosis and CBT groups were not significant. Physical functioning, body image, sexual functioning, arm symptoms, breast symptoms, future perspective, pain, digestive problems, and functional scale significantly changed in CBT and hypnosis groups (P < 0.05). Memory and social functioning; however, did not change in the groups and across the three groups. In addition, sleeping disorders and emotional malfunctioning were recovered only in the hypnosis group, which was statistically significant.

**Conclusion:** We found hypnosis exclusively effective on reducing certain problems of breast cancer patients, such as sleeping disorders and emotional malfunctioning; therefore, it is suggested as an efficient solution for these patients' problems.

*Keywords:* Breast cancer, Cognitive-behavioral therapy, Hypnosis, Chemotherapy, Quality of life

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# Introduction

Breast cancer is the most prevalent cancer and the first reason for cancer mortality among women in the world.<sup>1,2</sup> The average annual reported incidence of primary breast cancer in women is 22.6 per 100,000.<sup>3</sup> Regularly, women receiving medical treatment for breast cancer report pain, fatigue, nausea, sleeping disorders, vomiting, and hot flashes.<sup>1,4,5</sup> Moreover, chemotherapy has negative effects on the quality of life (QoL) of women with breast cancer.<sup>5,6</sup> QoL in these cases is influenced by the nature of the disease or the side-effects of the medical treatment.7 Accordingly, it could be described as a subjective and multidimensional state of physical, emotional, occupational, social, cognitive functioning, vitality levels, pain, body image, sexuality, and spirituality.<sup>8</sup> Numerous scientific studies have focused on various therapeutic techniques and strategies aiming to improve the QoL in these patients including cognitive behavioral therapy (CBT) and hypnosis intervention, due to the negative side-effects of cancer treatment.<sup>6</sup>

Mixed findings on the outcomes of CBT in breast cancer settings were obtained through longterm studies.9 Anticipatory QoL, nausea, and vomiting in adult and pediatric cancer patients undergoing chemotherapy could be effectively controlled via CBT,<sup>9,10</sup> focusing on the relationship between the thoughts, patient's behaviors and feelings, and their role in creating specific symptoms.<sup>11</sup> Furthermore, we found hypnosis effective on managing different physical and psychological symptoms, including stress, hot flashes, anxiety, quality of sleep, fatigue, and pain in patients with breast cancer.<sup>12-15</sup> Hypnotic methods, involving relaxation, suggestion,16 and distracting imagery, are effective on pain management.<sup>17</sup> Distractions are prevented in this state of altered consciousness. This allows the patient to focus on a particular symptom, illness, or problem<sup>18</sup> and nearly 90% of them would prefer to use this technique for managing the side-effects associated with cancer treatment.<sup>19</sup> Hypnosis was also indicated to be effective on managing the different physical and psychological symptoms in patients with breast cancer, such as distress,<sup>20</sup> anxiety, fatigue, quality of sleep, and pain. Thus, we could consider it as a useful adjuvant therapy for controlling the pain and anxiety in cancer.<sup>12,13,21</sup> We conducted the present study to determine the impacts of CBT and hypnotherapy on the QoL, depression, and stress in women suffering from breast cancer during chemotherapy, in comparison with a control group receiving standard medical care.

# **Patients and Methods**

The present study is a pretest-posttest trial with a control group, which was conducted in 2018 in Imam Khomeini Hospital of Sari affiliated with Mazandaran University of Medical Sciences. Herein, we aimed to compare the effectiveness of cognitive-behavioral therapy and hypnosis therapy on improving the OoL and decreasing the depression and anxiety in patients with breast cancer undergoing chemotherapy. The trial protocol was recorded at the Iranian Clinical Trials Registry (IRCT201703161457N13; www.irct.ir) and consistent with the Declaration of Helsinki and its subsequent revisions. The patients were provided with enough information regarding the research protocol and their right to leave the trial at any time, and they were asked to give the written informed consent. The study was performed in 2018. The statistical population involved all the breast cancer patients referring to Imam Khomeini Hospital of Sari.

A total of 50 patients were assigned to three groups of CBT, hypnosis, and control, with respectively 15, 20, and 15 patients assigned to each group. We employed Schnur et al.'s<sup>22</sup> findings to determine the required sample size. Based on their findings, the effect of combining CBT and hypnosis on increasing positive emotions was 85% in the intervention group and 43% in the control group with a confidence interval of 95% and a test power of 80%, with 15 people in the control group and 15 people in each of the intervention groups. G-power was used to determine the sample size.

The inclusion criteria for this study included breast cancer diagnosis, writing literacy, physical ability to attend treatment sessions, being under chemotherapy, having hypnotic susceptibility degree of more than 5 scores in Spiegel test, participation in at least six sessions, and having being over 18 years old.

The exclusion criteria included attending concurrent psychotherapy sessions, using psychoactive drugs, acute psychiatric disorder according to the psychiatrist report of this study, illiteracy, having metastatic breast cancer, and having filled the questionnaire incompletely. *Procedure* 

Eight 1-hour treatment sessions were run for each of the hypnosis and CBT groups, with the control group not receiving any treatments. A trained therapist assisted the patients in understanding the treatment protocol. Written consent was obtained from all of the patients. They were matched according to their age, marital status, and degree of hypnosis ability.

Demographic, QoL, depression, and anxiety forms and questionnaires were completed by the patients at the beginning and end of the treatment, as well as six months post-treatment.

# Protocol of treatments

# A. CBT

The adopted CBT treatment protocol was as follows:<sup>12,23</sup>

1- Cancer story and emotional expression, attitude expression about the cause of the present disease, and self-attribution of the disease and



Figure 1. This figure shows the CONSORT diagram of patients' randomization, intervention, and analysis.

Variable		Group	<i>P</i> -value	
(	CBT*(N=15)	HYP**(N=20)	CONT***(N=15)	
Age (mean ± SD)	42(±7)	48(±11)	47(±8)	0.1
Marriage F (%)				
Married	13(86.7%)	18(90%)	15(100%)	0.6
Single /Divorced/Widowed	2(13.4%)	2(10%)	0(0)	
Job F (%)				
housewife	14(93.3)	18(90)	15(100)	0.5
Employed	1(6.7)	2(10)	0(0)	
Cancer duration months (mean $\pm$ S	<b>D)</b> 11(±4)	10(±6)	16(±13)	0.6
Mastectomy F (%)	2(13.3%)	6(40%)	1(5%)	0.4
Hypnos ability	7.3(±1.5)	6.8(±1.7)	$7.5(\pm 0.8)$	0.7
Stress	17 (±3)	16(±3)	16 (±2.5)	0.6
Depression	15(±3.4)	$16(\pm 3.5)$	15(±3.6)	0.5
*Cognitive- behavioral therapy; **Hypnotism;	***Control			

Table1. Basic demographic and clinical characteristics of the patients in the three group

relaxation.

2- Negative thoughts, their recognition, and determining home assignments.

3- Reviewing homework and discussing the impact of thoughts on feelings.

4- Confrontation with the negative thoughts and homework assignments reviewing.

5- Improving interpersonal relationships and coping with the stigma of the disease.

6- Negative thought control, social, and

problem-solving skills.

- 7- Summarizing the previous sessions.
- 8- Coping with uncertainty, and relaxation.

## B. Hypnotherapy

The hypnotherapy protocol was as follows:<sup>24,25</sup>

1-Explaining the concept and process of hypnosis, safe space imagery with egostrengthening, and reducing negative thoughts associated with feeling guilty for having caused the disease.



**Figure 2.** This figure shows sleep problem trends over time in the various groups (\*The first visit was after 8 weeks and the second was after 6 months).

CBT: Cognitive behavioral therapy

Variables		Time				Group effect	Interaction effect
		First visit Mean(SD)	Follow up after 8weeks Mean(SD)	Follow up after 6 months Mean(SD)			
Stress	CBT	17 (±3.1)	13.7 (±2.5)	13.4(±2.3)	0.001	0.4	0.001
	HYP	16(±3.3)	15.9(±3)	15.7(±3)	0.005		
	CONT	16.1(±2.5)	16.1(±2.5)	16(±2.3)	0.4		
Depression	CBT	14.6(±3.4)	12.3(±2)	11(±2)	0.001	0.02	0.001
	HYP	16(±3.5)	16(±3.4)	15.4(±3)	0.002		
	CONT	15.1(±3.6)	15.1(±3.6)	15(±3.6)	0.4		

**Table2.** Stress and depression among the participants (scores at baseline and time intervals of 6, 12 and 29 weeks after treatment) in the three groups

2- Mental imagery of chemotherapy and feelings of pain and nausea and cramps, and hypnotic visualization of the increase in body immunity level.

3- Mental imaging of chemotherapy, coping with its side-effects, and ego-strengthening.

4- Strengthening ego, improving body image, and increasing sexual desire.

5- Imagery of increasing the control of treatment complications and increasing the immunity level.

6- Reducing anxiety caused by thoughts of recurrence of the disease and how to cope with it.

7- Self-loving and loving others, self-forgiving and forgiving others, and increasing the level of body immunity. 8- Promoting self-strength, increasing immunity level, and embarking on the future road of health and well-being.

# Hypnotizability

Hypnotizability was evaluated via Spiegel test including the eye up-gaze (0-4 score), The eye roll up (0-4 score), and Lucy (0-2 score).<sup>26</sup> The score of Hypnotizability was recorded on a scale of 0-10, with 10 being the most roll/most susceptibility to hypnosis.<sup>27</sup>

### Instruments

### Demographic questionnaire

The questionnaire included age, marriage, education, occupation, spouse's education, number of children, stage of the disease, and history of chemotherapy.



Figure 3. This figure shows memory problem trends over time in the various groups (\*The first visit was after 8 weeks and the second was after 6 months).

### QoL questionnaires

We used two QoL questionnaires in this research:

1. The European Organization for Research and Treatment of Breast Cancer-specific QoL Questionnaire (EORTC – BR 23): This questionnaire includes 23 questions, consisting of five functional scales (sexuality, body image, sexual pleasure, future perspective) and four symptom scales (side-effects of systemic therapy, breast symptoms, arm symptoms, and discomfort due to hair loss).<sup>28,29</sup> In Iran, the Cronbach's alpha coefficient for multipart scales of EORTC QLQ-BR23 varies from 0.63 to 0.95 in the baseline and from 0.75 to 0.92 in the follow-up.<sup>30</sup>

2. The European Organization for Research and Treatment of Cancer QoL Questionnaire (EORTC QLQ-C30): This questionnaire comprises 30 questions, including five functional scales (physical, role-playing, emotional, cognitive, and social), and nine symptom scales (fatigue, nausea and vomiting, pain, sleeping disorders, insomnia, loss of appetite, constipation, diarrhea, and occupational problems).<sup>31,32</sup> Montazeri et al. and Hosseini et al. validated the Persian version of this questionnaire in 2007.<sup>30,33</sup> *Anxiety and Depression Scale* 

# The Hospital Anxiety and Depression Scale (HADS)

This scale includes seven questions concerning anxiety and seven questions concerning depression.<sup>34</sup> The Cronbach's alpha of the Persian version was obtained at 0.86 for the depression subscale and 0.78 for the anxiety subscale.<sup>35</sup> *Statistical analysis* 

To assess whether the data were normally distributed, we utilized the Shapiro-Wilk test. Descriptive baseline characteristics for the comparison among the three groups were tabulated as Mean (SD) or as percentages. The comparison between these three groups for the categorical data was statistically analyzed using chi- square or Fisher-exact test. We employed intention-totreat analysis for examining the initial efficacy data on the hypnosis and CBT functions. Using General Linear Model (GLM), the status of the outcomes across the three groups was examined via repeated measurement ANOVA test. The type



Figure 4. This figure shows body image problem trends over time in the various groups. (\*The first visit was after 8 weeks and the second was after 6 months).

of intervention (CBT or Hypnosis) was considered as between-subject factor, and the evaluation time as the within-subject factor. The time groups (interaction term) was measured as group differences (among the three groups). Mauchley's sphericity test was applied for compound symmetry assumption. A *P*- value of 0.05 or less was considered statistically significant. Using IBM SPSS12 statistics version 16 and Stata version, we analyzed the obtained data.

### Results

### **Participants**

During this study, a total of 120 patients referring to our clinic were screened. Among these, 20 patients did not meet the eligibility criteria and 50 patients failed to participate in the study. The remaining 50 patients were assigned to three groups. A total of 50 patients participated in the present study and the data from all these patients were analyzed (Figure 1).

Ultimately, 50 women aged 25 to 65 (average 46.3±9 years of age) were assigned to three groups of 15, 20, and 15 patients (pertaining to CBT, Hypnosis, and control groups, respectively).<sup>32</sup> (64%) of the participants were in primary and guidance education, 47 patients (94%) were married, and 47 (94%) were house-wives. The average number of the children in the study groups was 2.4(±9) with a duration of cancer diagnosis of 12.4(±9) months. Mean of hypnosis ability in the patients was 7(±1.4); in addition, 9(18%) of them had undergone mastectomy. Table 1 represents the basic demographic and clinical characteristics of the patients in the three groups. Based on table 1, there were no significant



Figure 5. This figure shows the global quality of life trends over time in the various groups. (\*The first visit was after 8 weeks and the second was after 6 months).

Table3. Score changes in the symptoms subscale of the quality of life in the participants (scores at baseline and time intervals of six weeks and six months after treatment) in the three groups

Variables	bles Time				Group	Interaction
	First visit	Follow-up after 8 weeks Moon(SD)	Follow-up after 6 months Meen(SD)	cheet	eneer	eneer
Physical functioning	Mean(SD)	Mean(SD)	Mean(SD)			
CBT	21(+1.4)	20.6(+3.8)	20(+3.0)	0.001	0.5	0.001
	$21(\pm 1.4)$ $21(\pm 4.6)$	$20.0(\pm 3.8)$ 10.2( $\pm 2.2$ )	$20(\pm 3.3)$ 17.0( $\pm 2.7$ )	0.001	0.5	0.001
	$21(\pm 4.0)$ 18 0(+6.4)	$19.3(\pm 5.2)$ 18.0(+6.4)	$1/.9(\pm 2.7)$ 18.7(+6.2)	0.001		
Dodu image	$18.9(\pm 0.4)$	$18.9(\pm 0.4)$	$18.7(\pm 0.2)$	0.1		
Body Image	0.1(+2.0)	7.9(+1.6)	$\overline{a}$	0.001	0.01	0.04
CBI	$9.1(\pm 2.8)$	7.8(±1.6)	$7.7(\pm 1.5)$	0.001	0.01	0.04
HYP	8./(±3.6)	8.4(±3.2)	7.5(±2.4)	0.007		
CONT	$5.9(\pm 2.3)$	$5.9(\pm 2.3)$	$6(\pm 1.9)$	0.7		
Sexual functioning						
CBT	$8.2(\pm 1.3)$	$8.2(\pm 1.3)$	$8.7(\pm 1)$	0.02	0.9	0.1
HYP	$8(\pm 1.4)$	$8(\pm 1.4)$	$8.7(\pm 1.4)$	0.01		
CONT	$8.3 \pm (0.8)$	$8.3(\pm 0.8)$	8.3(±0.7)	0.1		
Arm symptoms						
CBT	7(±2.5)	6.6(±2)	6.5(±2)	0.02	0.03	0.2
НҮР	5.7(±1.8)	$5.2(\pm 1.4)$	4.8(±1.2)	0.004		
CONT	$6(\pm 1.3)$	$5.9(\pm 1.3)$	$5.9(\pm 1.3)$	0.2		
Breast symptoms			( )			
CBT	$8.3(\pm 4)$	$7.9(\pm 3.5)$	$8(\pm 3)$	0.02	0.8	0.2
НУР	8(±3.6)	$7.3(\pm 2.5)$	$6.7(\pm 2)$	0.004		
CONT	8(+2.6)	8(+2.5)	8(+25)	0.001		
Future perspective	0(-2.0)	0(-2.5)	0(-2.5)	0.1		
CBT	27(+13)	2(+0.8)	1.7(+0.7)	0.002	0.6	0.03
	$2.7(\pm 1.3)$ $2.2(\pm 1)$	$2(\pm 0.8)$ $2(\pm 0.8)$	$1.7(\pm 0.7)$ $1.8(\pm 0.7)$	0.002	0.0	0.05
CONT	$2.2(\pm 1)$ 1.0( $\pm 1$ )	$2(\pm 0.8)$ 1 0(±1)	$1.0(\pm 0.7)$ $1.7(\pm 0.8)$	0.02		
CONT Emotional functioning	$1.9(\pm 1)$	$1.9(\pm 1)$	$1.7(\pm 0.8)$	0.14		
CDT	11.5(+2.0)	11(12.4)	11(12.4)	0.05	0.2	0.09
CBI	$11.5(\pm 3.8)$	$11(\pm 3.4)$	$11(\pm 3.4)$	0.05	0.5	0.08
HYP	$10.6(\pm 3.1)$	$9.4(\pm 2.1)$	$9.4(\pm 2.1)$	0.001		
CONT	9.6(±2.6)	9.5(±2.6)	9.5(±2.6)	0.4		
Cognitive functioning		/	/			
CBT	$2.4(\pm 1.5)$	$2.3(\pm 1.4)$	$2.3(\pm 1.3)$	0.2	0.3	0.9
НҮР	$2.8(\pm 1)$	$2.7(\pm 1)$	$2.6(\pm 0.9)$	0.2		
CONT	$2.2(\pm 0.8)$	$2.2\pm(0.8)$	$2.1(\pm 0.6)$	0.1		
Social functioning						
CBT	$2(\pm 1.2)$	$1.8(\pm 0.9)$	$1.8(\pm 0.9)$	0.05	0.16	0.6
HYP	$2.5(\pm 1.1)$	$2.4(\pm 1)$	$2.4(\pm 1)$	0.05		
CONT	$1.9(\pm 0.9)$	$1.8(\pm 0.9)$	$1.8(\pm 0.9)$	0.4		
Fatigue						
CBT	$3(\pm 1.2)$	$3(\pm 1)$	$2.8(\pm 1)$	0.02	0.09	0.6
НҮР	$2.6(\pm 1)$	$2.4(\pm 0.8)$	$2.2(\pm 0.9)$	0.02		
CONT	$2.4(\pm 0.8)$	$2.4(\pm 0.8)$	$2.3(\pm 0.6)$	0.14		
Pain	()	()	()			
CBT	22(+13)	2(+1, 1)	1.9(+1)	0.04	0.4	0.5
HVP	$2.2(\pm 1.5)$ 2.2(+1)	$2(\pm 1.1)$ 2 1(+0.8)	2(+0.7)	0.04	0.1	0.5
CONT	$1.7(\pm 0.6)$	$1.7(\pm 0.6)$	$2(\pm 0.7)$ 1 6(+0 5)	0.04		
Sloop problems	1.7(±0.0)	1.7(±0.0)	1.0(±0.5)	0.1		
	$2.5(\pm 1)$	$22(\pm 0.0)$	$22(\pm 0.8)$	0.1	0.3	0.02
	$2.3(\pm 1)$	$2.3(\pm 0.9)$	$2.3(\pm 0.8)$	0.1	0.5	0.02
	$2.9(\pm 1.1)$	$2.7(\pm 0.8)$	$2.3(\pm 0.9)$	0.01		
CONT	$2.1(\pm 0.8)$	$2.2(\pm 0.8)$	$2.2(\pm 0.8)$	0.4		
Digestive problems				0.001		
CBT	$12.5(\pm 3.5)$	$11.6(\pm 3.1)$	$11.3(\pm 3.1)$	0.001	0.007	0.004
НҮР	$10.4(\pm 4)$	8.7(±2)	7.6(±2)	0.001		
CONT	9.4(±2.5)	$9.3(\pm 2.3)$	9.3(±2.3)	0.14		
Functional scale						
CBT	11.9(±3.2)	11.5(±2.7)	11.4(±2.6)	0.006	0.6	0.02
НҮР	11.6(±2.9)	11.2(±2.4)	10.5(±2.1)	0.001		
CONT	$10.5(\pm 3.9)$	$10.4(\pm 3.7)$	$10.5(\pm 3.7)$	0.4		
Global OoL	( )	( )				
CRT	$33(\pm 10)$	$(1)(+1)^{(+1)}$	(1, 2(+1))	0.004	0.1	0.3
	$3.5(\pm 1.9)$	$4.1(\pm 1.3)$	(+.3(+1))	0.004	0.1	0.5
HTP	3.5(±1.8)	$4(\pm 1.2)$	$4.3(\pm 1)$	0.002		
CONT	$3.8(\pm 1.5)$	$4(\pm 1.2)$	$4.1(\pm 1.1)$	0.08		

\*Interaction between time and group; Data are expressed as the mean (SD) CBT: Cognitive behavioral therapy; HYP: Hypnotism; CONT: Control; QoL: Quality of life differences regarding the average age, marital status, profession, and other characteristics of the patients.

### Stress

According to table 2, the differences concerning stress reduction in the three study groups were statistically significant (group effect, P = 0.4, and 0.001, respectively). In CBT and hypnosis groups, the stress differences were statistically significant (between effect, P=0.001, and 0.005), while they were not statistically significant in the control group (between effect, P=0.4).

# Depression

Table 2 depicts that the differences regarding depression reduction in the three groups were statistically significant (group effect, P=0.02 and 0.001, respectively). Furthermore, depression differences in CBT and hypnosis groups were statistically significant (between effect, P=0.001 and 0.002, respectively); whereas, it was not statistically significant in the control group (between effect, P=0.4).

## QoL

Based on table 3 and figures 2-5, physical functioning, body image, sexual functioning, arm symptoms, breast symptoms, future perspective, emotional functioning, social functioning, fatigue, pain, digestive problems, functional scale, and global QoL improved in the CBT and hypnosis groups (P < 0.05), which was statistically significant. Cognitive functioning, however, was not found to be statistically significant within and between the three groups of study. Additionally, insomnia recovery was found to be statistically significant only in the hypnosis group. Memory and social functioning; however, were not found to be significant in the groups and among the three of them. In addition, emotional functioning; was recovered only in the hypnosis group, which was statistically significant.

## Discussion

Our study revealed an improvement in QoL and a decrease in the chemotherapy side-effects in the patients in two intervention groups. However, the differences were not significant between the groups. Several studies have examined the effectiveness of CBT or hypnotherapy on minimizing the side-effects of chemotherapy in breast cancer patients. A study in the United States reported that the group undergone the combined hypnotherapy and CBT experienced significantly less fatigue and muscle weakness at all time-points.<sup>36</sup> On top of that, in another study, eight women under breast cancer treatment received self-hypnosis training for symptom management. Significant pre- to posttreatment reductions in pain intensity, fatigue, and sleep problems were revealed via analyses, and pain intensity was associated to the decrease from post-treatment to 6-month follow-up.<sup>37</sup> These findings are consistent with an earlier study on hypnosis with CBT in reducing fatigue in breast cancer patients,<sup>12,38</sup> which is compatible to our findings. Moreover, a clinical trial compared the effectiveness of combining four sessions of the hypnosis with CBT regarding the management of depression, pain, and distress with education control in 44 cancer patients. An improvement in these variables was reported.<sup>39</sup> Fatigue, depression and pain also decreased in the CBT and hypnosis groups in our study.

In another study, short-term CBT improved in Hamilton's anxiety scale.<sup>40</sup> CBT intervention in our work also demonstrated a significant improvement in HAD's anxiety scale. In addition, in a non-randomized trial with the control group, the effect of group cognitive therapy in breast cancer patients under chemotherapy showed a significant decrease in anxiety and depression in the intervention group.<sup>41</sup> According to our results, there was also a significant decrease in anxiety and depression in the CBT groups.

On the other hand, the meta-analysis of six pooled studies did not demonstrate any improvement in QOL in breast cancer survivors via CBT. The interpretation of these results, however, requires further attenion.<sup>9</sup> In another study, hypnosis was reported as an effective intervention for reducing distress, pain, and other symptoms and side-effects associated with cancer and its treatment.<sup>19</sup> Furthermore, a quasiexperimental study with a control group in Iranian breast cancer patients investigated the effects of CBT on anxiety, depression, and stress in 24 women with breast cancer throughout 10 sessions. CBT had significant effects on reducing these variables in the trial group comparing with the control group.<sup>42</sup> Similarly, in our research, pain, anxiety, depression, and stress declined in CBT and hypnosis group.

Furthermore, in a quasi-experimental study<sup>43</sup> on 55 Iranian breast cancer patients, which focused on 2 guided imagery tracks, the frequency and severity of nausea and vomiting declined in the patients comparing to those in the control group. We also observed a decrease in nausea and vomiting. Moreover, in a quasi-experimental study among the Iranian breast cancer patients undergoing chemotherapy, family counseling led to the reduction of sleeping disorders, constipation, fatigue, worrying about the hair-loss, breast and arms related symptoms ,vomiting and nausea, pain, painful breathing, lack of appetite, diarrhea, and financial problems,<sup>44</sup> which is compatible to our findings. Additionally, in a trial, two groups of 100 breast cancer patients were enrolled with cognitive behavioral intervention, the scores of stress in the control group were significantly higher than those in the intervention group.<sup>45</sup> In the current study, we also observed a reduction in stress with CBT.

In a meta-analysis randomized controlled trial in women with metastatic breast cancer, psychological interventions were effective on enhancing the QoL, relationships, social activities, and sleep quality, and on alleviating the pain,<sup>46</sup> which is in accordance with our results. In a systematic review,47 13 randomized clinical trials (RCT)s with 1357 patients were involved. Hypnosis decreased the pain and distress in the women undergoing diagnostic breast biopsy (three RCTs); one RCT on breast cancer surgery was affected by hypnosis on pain, distress, fatigue, and nausea. Hypnosis combined with CBT improved the distress and fatigue in the women undergoing radiotherapy (three RCTs). Hypnosis also improved distress in three RCTs. Three RCTs on women with metastatic breast cancer revealed certain effects on pain and distress. Moreover, Richardson and colleagues<sup>48</sup> systematically reviewed randomized controlled trials of hypnosis for vomiting and nausea controlling attributed to chemotherapy. In a quasi-experimental design with 40 breast cancer women using EORTC QLQ-C3, the hypnotherapy group also showed a statistically significant improvement and a large effect size on the cognitive functioning and social functioning scales compared with the control group. The physical functioning, role functioning, and QoL scales illustrated an improvement with a medium effect size, yet the changes were not statistically significant.<sup>49</sup> In the current work, we observed an improvement in these OoL variables.

In a pilot clinical trial with 71 cancer patients, brief behavioral therapy on insomnia improved QoL and decreased insomnia more efficiently than the healthy-eating control intervention; the difference herein was significant.<sup>50</sup> Cancer patients struggle with insomnia, which impairs their QoL.<sup>50</sup> In our study, sleeping disorders decreased in CBT group.

In a quasi-experimental design, with the control group receiving standard medical care (n = 20)or a hypnotherapy group (n = 20) using EORTC QLQ-C30, the patients' QoL was investigated. A statistically significant improvement and a large effect size on the cognitive functioning and social functioning scales were found in the hypnotherapy group compared to the control group. The scales of QoL improved with a medium effect size; however, the changes were not statistically significant. Moreover, social activities, mood, sleep, concentration, relations with others, sexual activity, life enjoyment, and the overall QoL improved.<sup>51</sup> The enhancement observed in the cognitive functioning and social functioning scales suggests the improved QoL in breast cancer patients during chemotherapy with hypnotherapy.52

Following these interventions,<sup>53</sup> the physical functioning, social functioning scales and QoL of the patients improved in our study. The improved physical functioning is of great importance, since it makes it possible for the patients to achieve a greater level of independence in their routine activities, for instance getting up, getting dressed, and eating. It also helps the patients to be capable of integrating into their work and social life and thereby, improving their life quality.

## Conclusions

Considering the nature of cancer and severe complications of chemotherapy, including weakness and fatigue, it is difficult to encourage patients to attend psychotherapy sessions and participate in challenging programs. This made the randomization impossible. Thus, a larger sample size is recommended for future studies. Furthermore, even though the overall sociodemographic characteristics intervention groups were similar to the control group, we did not utilize a random sampling method for the participant recruitment, which is an advantage of our work.

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# **Conflicts of Interest**

None declared.

# References

- Söderman M, Friberg E, Alexanderson K, Wennman-Larsen A. Women's experiences of encounters with healthcare professionals' regarding work after breastcancer surgery and associations with sickness absence: a 2-year follow-up cohort study. *Support Care Cancer*. 2019;27(4):1197-206. doi: 10.1007/s00520-018-4453-1.
- Fouladi N, Amani F, Sadeghi Movahed F, Ali-Mohammadi H, Pourfarzi F, Parvizi F. Perceived attentional function and related factors in women following breast cancer surgery. *Middle East J Cancer*. 2016;7 (1): 41-5.
- Jazayeri SB, Saadat S, Ramezani R, Kaviani A. Incidence of primary breast cancer in Iran: Ten-year national cancer registry data report. *Cancer Epidemiol.* 2015;39(4):519-27. doi: 10.1016/j.canep.2015.04.016.
- Hart SL, Hoyt MA, Diefenbach M, Anderson DR, Kilbourn KM, Craft LL, et al. Meta-analysis of efficacy of interventions for elevated depressive symptoms in adults diagnosed with cancer. *J Natl Cancer Inst.* 2012; 104(13): 990-1004.
- 5. Ewertz M, Jensen AB. Late effects of breast cancer treatment and potentials for rehabilitation. *Acta Oncologica (Stockholm, Sweden)*. 2011;50(2):187-93.

doi: 10.3109/0284186X.2010.533190.

- Härtl K, Engel J, Herschbach P, Reinecker H, Sommer H, Friese K. Personality traits and psychosocial stress: quality of life over 2 years following breast cancer diagnosis and psychological impact factors. *Psychooncology*. 2010;19(2):160-9. doi: 10.1002/pon. 1536.
- Pruthi DS, Ahmad M, Gupta M, Bansal S, Nautiyal V, Saini S. Assessment of quality of life in resectable gastric cancer patients undergoing chemoradiotherapy as adjuvant treatment. *South Asian J Cancer.* 2018;7(1):16-20. doi: 10.4103/sajc.sajc\_196\_17.
- Osoba D. Health-related quality of life and cancer clinical trials. *Ther Adv Med Oncol.* 2011;3(2):57-71. doi: 10.1177/1758834010395342.
- Zhang M, Huang L, Feng Z, Shao L, Chen L. Effects of cognitive behavioral therapy on quality of life and stress for breast cancer survivors: a meta-analysis. *Minerva Med.* 2017;108(1):84-93. doi: 10.23736/S0026 -4806.16.04528-6.
- Okuyama T, Akechi T, Mackenzie L, Furukawa TA. Psychotherapy for depression among advanced, incurable cancer patients: A systematic review and meta-analysis. *Cancer Treat Rev.* 2017;56:16-27. doi: 10.1016/j.ctrv.2017.03.012.
- Cuijpers P, Cristea IA, Karyotaki E, Reijnders M, Huibers MJ. How effective are cognitive behavior therapies for major depression and anxiety disorders? A meta-analytic update of the evidence. *World Psychiatry.* 2016;15(3):245-58. doi: 10.1002/wps. 20346.
- Montgomery GH, David D, Kangas M, Green S, Sucala M, Bovbjerg DH, et al. Randomized controlled trial of a cognitive-behavioral therapy plus hypnosis intervention to control fatigue in patients undergoing radiotherapy for breast cancer. *J Clin Oncol.* 2014;32(6):557-63. doi: 10.1200/JCO.2013.49.3437.
- Elkins GR, Fisher WI, Johnson AK, Carpenter JS, Keith TZ. Clinical hypnosis in the treatment of postmenopausal hot flashes: a randomized controlled trial. *Menopause*. 2013;20(3):291-8. doi: 10.1097/ GME.0b013e31826ce3ed.
- Sohl SJ, Stossel L, Schnur JB, Tatrow K, Gherman A, Montgomery GH. Intentions to use hypnosis to control the side effects of cancer and its treatment. *Am J Clin Hypn.* 2010;53(2):93-100.
- Corbett TK, Groarke A, Devane D, Carr E, Walsh JC, McGuire BE. The effectiveness of psychological interventions for fatigue in cancer survivors: systematic review of randomised controlled trials. *Syst Rev.* 2019;8(1):324. doi: 10.1186/s13643-019-1230-2.
- 16. Gadisa DA, Gebremariam ET, Ali GY. Reliability and validity of Amharic version of EORTC QLQ-C30 and QLQ-BR23 modules for assessing health-related quality of life among breast cancer patients in Ethiopia. *Health Qual Life Outcomes.* 2019;17(1):182. doi:

10.1186/s12955-019-1257-z.

- Pope J, Legler A. Integrative therapies for pain modulation. In: Gulati A, Puttanniah V, Bruel BM, Rosenberg WS, Hung JC, editors. Essentials of interventional cancer pain management; 2019. Springer International Publishing: NewYork.p.507-511.
- Elkins GR, Fisher WI, Johnson AK. Hypnosis for hot flashes among postmenopausal women study: a study protocol of an ongoing randomized clinical trial. *BMC Complement Altern Med.* 2011;11:92. doi: 10.1186/ 1472-6882-11-92.
- Paredes AC, Costa P, Fernandes S, Lopes M, Carvalho M, Almeida A, et al. Effectiveness of hypnosis for pain management and promotion of health-related quality-of-life among people with haemophilia: a randomised controlled pilot trial. *Sci Rep.* 2019;9(1): 13399. doi: 10.1038/s41598-019-49827-1.
- Montgomery GH, Sucala M, Dillon MJ, Schnur JB. Cognitive-behavioral therapy plus hypnosis for distress during breast radiotherapy: A randomized trial. *Am J Clin Hypn.* 2017;60(2):109-22. doi: 10.1080/ 00029157.2017.1335635.
- Brugnoli MP, Pesce G, Pasin E, Basile MF, Tamburin S, Polati E. The role of clinical hypnosis and self-hypnosis to relief pain and anxiety in severe chronic diseases in palliative care: a 2-year long-term follow-up of treatment in a nonrandomized clinical trial. *Ann Palliat Med.* 2018;7(1):17-31. doi: 10.21037/apm. 2017.10.03.
- Schnur JB, David D, Kangas M, Green S, Bovbjerg DH, Montgomery GH. A randomized trial of a cognitive-behavioral therapy and hypnosis intervention on positive and negative affect during breast cancer radiotherapy. *J Clin Psychol.* 2009;65(4):443-55. doi: 10.1002/jclp.20559.
- 23. Zhang P, Mo L, Torres J, Huang X. Effects of cognitive behavioral therapy on psychological adjustment in Chinese pediatric cancer patients receiving chemotherapy: A randomized trial. *Medicine* (*Baltimore*). 2019;98(27):e16319. doi: 10.1097/MD. 000000000016319.
- 24. Grégoire C, Faymonville ME, Vanhaudenhuyse A, Charland-Verville V, Jerusalem G, Bragard I. Randomized controlled trial of an 8-week intervention combining self-care and hypnosis for post-treatment cancer patients: study protocol. *BMC Cancer*. 2018;18(1):1113. doi: 10.1186/s12885-018-5046-6.
- 25. Willmarth EK. Clinical hypnosis in pain therapy and palliative care: A handbook of techniques for improving the patient's physical and psychological well-being by Brugnoli, Maria Paola. *Am J Clin Hypn.* 2017;59(3): 318-20.
- Frischholz EJ, Nichols LE. A historical context for understanding "An eye roll test for hypnotizability" by Herbert Spiegel, M.D. *Am J Clin Hypn*. 2010;53(1): 3-13.

- David D, Cotet C, Matu S, Mogoase C, Stefan S. 50 years of rational-emotive and cognitive-behavioral therapy: A systematic review and meta-analysis. *J Clin Psychol.* 2018;74(3):304-18. doi: 10.1002/jclp. 22514.
- Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst.* 1993;85(5):365-76.
- 29. Laghousi D, Jafari E, Nikbakht H, Nasiri B, Shamshirgaran M, Aminisani N. Gender differences in health-related quality of life among patients with colorectal cancer. *J Gastrointest Oncol.* 2019;10(3): 453-61. doi:10.21037/jgo.2019.02.04.
- Montazeri A, Harirchi I, Vahdani M, Khaleghi F, Jarvandi S, Ebrahimi M, et al. The EORTC breast cancer-specific quality of life questionnaire (EORTC QLQ-BR23): translation and validation study of the Iranian version. *Qual Life Res.* 2000;9(2):177-84.
- Kemmler G, Gamper E, Nerich V, Norman R, Viney R, Holzner B, et al. German value sets for the EORTC QLU-C10D, a cancer-specific utility instrument based on the EORTC QLQ-C30. *Qual Life Res.* 2019;28(12): 3197-211. doi:10.1007/s11136-019-02283-w.
- 32. McTaggart-Cowan H, King MT, Norman R, Costa DSJ, Pickard AS, Regier DA, et al. The EORTC QLU-C10D: The Canadian valuation study and algorithm to derive cancer-specific utilities from the EORTC QLQ-C30. *MDM Policy Pract.* 2019;4(1):23814683 19842532. doi: 10.1177/2381468319842532.
- 33. Hosseini SA, Zahrooni N, Ahmadzadeh A, Ahmadiangali K, Assarehzadegan MA. The effect of CoQ(10) supplementation on quality of life in women with breast cancer undergoing tamoxifen therapy: A double-blind, placebo-controlled, randomized clinical trial. *Psychol Res Behav Manag.* 2020;13:151-9.
- Hassannia L, Taghizadeh F, Moosazadeh M, Zarghami M, Taghizadeh H, Fathi Dooki A, et al. Anxiety and depression in health workers and general population during COVID-19 epidemic in IRAN: A web-based cross-sectional study. [Internet] medRxiv - Psychiatry and Clinical Psychology; 2020. doi: 10.1101/2020.05. 05.20089292.
- 35. Montazeri A, Vahdaninia M, Ebrahimi M, Jarvandi S. The Hospital Anxiety and Depression Scale (HADS): translation and validation study of the Iranian version. *Health Qual Life Outcomes*. 2003;1:14.
- Jong MC, Boers I, van Wietmarschen H, Busch M, Naafs MC, Kaspers GJL, et al. Development of an evidence-based decision aid on complementary and alternative medicine (CAM) and pain for parents of children with cancer. *Support Care Cancer*. 2020;28(5):2415-29. doi: 10.1007/s00520-019-05058-8.

- Jensen MP, Gralow JR, Braden A, Gertz KJ, Fann JR, Syrjala KL. Hypnosis for symptom management in women with breast cancer: a pilot study. *Int J Clin Exp Hypn.* 2012;60(2):135-59. doi: 10.1080/00207144. 2012.648057.
- Montgomery GH, Kangas M, David D, Hallquist MN, Green S, Bovbjerg DH, et al. Fatigue during breast cancer radiotherapy: an initial randomized study of cognitive-behavioral therapy plus hypnosis. *Health Psychol.* 2009;28(3):317-22. doi: 10.1037/a0013582.
- 39. Mendoza ME, Capafons A, Gralow JR, Syrjala KL, Suárez-Rodríguez JM, Fann JR, et al. Randomized controlled trial of the Valencia model of waking hypnosis plus CBT for pain, fatigue, and sleep management in patients with cancer and cancer survivors. *Psychooncology*. 2017;26(11):1832-8. doi: 10.1002/pon.4232.
- Greer JA, Traeger L, Bemis H, Solis J, Hendriksen ES, Park ER, et al. A pilot randomized controlled trial of brief cognitive-behavioral therapy for anxiety in patients with terminal cancer. *Oncologist*. 2012;17(10):1337-45. doi: 10.1634/theoncologist.2012-0041.
- 41. Kalke K, Ginossar T, Bentley JM, Carver H, Shah SFA, Kinney AY. Use of evidence-based best practices and behavior change techniques in breast cancer apps: Systematic analysis. *JMIR Mhealth Uhealth*. 2020;8(1):e14082. doi:10.2196/14082.
- Joly F, Lange M, Dos Santos M, Vaz-Luis I, Di Meglio A. Long-term fatigue and cognitive disorders in breast cancer survivors. *Cancers (Basel)*. 2019;11(12). pii: E1896. doi: 10.3390/cancers11121896.
- 43. Hosseini M, Tirgari B, Forouzi MA, Jahani Y. Guided imagery effects on chemotherapy induced nausea and vomiting in Iranian breast cancer patients. *Complement Ther Clin Pract.* 2016;25:8-12. doi: 10.1016/j.ctcp. 2016.07.002.
- Tran TH, Trinh NL, Hoang Y, Nguyen TL, Vu TT. Health-related quality of life among vietnamese breast cancer women. *Cancer Control.* 2019;26(1): 1073274819862787. doi: 10.1177/1073274819862787.
- 45. Burm R, Thewes B, Rodwell L, Kievit W, Speckens A, van de Wal M, et al. Long-term efficacy and costeffectiveness of blended cognitive behavior therapy for high fear of recurrence in breast, prostate and colorectal Cancer survivors: follow-up of the SWORD randomized controlled trial. *BMC Cancer*. 2019;19(1):462. doi: 10.1186/s12885-019-5615-3.
- Mustafa M, Carson-Stevens A, Gillespie D, Edwards AG. Psychological interventions for women with metastatic breast cancer. *Cochrane Database Syst Rev.* 2013;(6):CD004253. doi: 10.1002/14651858. CD004253.pub4.
- 47. Cramer H, Lauche R, Paul A, Langhorst J, Kümmel S, Dobos GJ. Hypnosis in breast cancer care: a systematic review of randomized controlled trials.

Integr Cancer Ther. 2015;14(1):5-15. doi: 10.1177/1534735414550035.

- 48. Richardson J, Smith JE, McCall G, Richardson A, Pilkington K, Kirsch I. Hypnosis for nausea and vomiting in cancer chemotherapy: a systematic review of the research evidence. *Eur J Cancer Care (Engl)*. 2007;16(5):402-12.
- 49. Grégoire C, Nicolas H, Bragard I, Delevallez F, Merckaert I, Razavi D, et al. Efficacy of a hypnosisbased intervention to improve well-being during cancer: a comparison between prostate and breast cancer patients. *BMC Cancer*. 2018;18(1):677. doi: 10.1186/s12885-018-4607-z.
- Palesh O, Scheiber C, Kesler S, Gevirtz R, Heckler C, Guido JJ, et al. Secondary outcomes of a behavioral sleep intervention: A randomized clinical trial. *Health Psychol.* 2019;38(3):196-205. doi: 10.1037/hea0000700.
- 51. Elkins G, Marcus J, Stearns V, Hasan Rajab M. Pilot evaluation of hypnosis for the treatment of hot flashes in breast cancer survivors. *Psychooncology*. 2007;16(5): 487-92.
- 52. Guarino A, Polini C, Forte G, Favieri F, Boncompagni I, Casagrande M. The effectiveness of psychological treatments in women with breast cancer: A systematic review and meta-analysis. *J Clin Med.* 2020;9(1):209.
- 53. Zarghami M, Taghizadeh F, Sharifpour A, Alipour A: Efficacy of guided self-change for smoking cessation in chronic obstructive pulmonary disease patients: A randomized controlled clinical trial. *Tob Induc Dis.* 2019; 17(12):90.