Cancer Related Fatigue and Upper Limb Disabilities Cannot Improve after 6 Weeks Resistance Training with Thera-Band in Breast Cancer Survivors

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ABSTRACT

Aim. Breast cancer and its treatments lead to cancer related fatigue and upper limb disabilities. On the other hand, resistance training has positive benefits for breast cancer survivors. Thus, the aim of present study was to clarify the effect of resistance training with Thera – Band on CRF and upper limb disabilities in breast cancer survivors. Methods. Fifty women with breast cancer aged 29-65 were divided in to 2 groups: 1) resistance training with Thera- Band group (n=25) and 2) control group (n=25). Resistance training with Thera- Band group, after 5 minutes warm up, were performed the 9 resistance training with Thera – Band, from 8 to 12 repetitions and 2 sets in the first two weeks, 8 to 12 repetitions and 3 sets in the second two weeks and 8 to 12 repetitions and 4 sets in the third two weeks. The rest between each set was started from 90 seconds in the first week and was decreased to 45 seconds in the sixth week. Control group didn’t have any supervised or regular physical activity. Cancer related fatigue (CRF) and upper limb disabilities were surveyed by Piper Fatigue Scale and DASH questionnaire, respectively. Data were analyzed using by 2-way ANOVA (p≤0.05). Statistical Results. The findings of this study demonstrated that 6 weeks resistance training by Thera – Band has no significant effect on CRF and upper limb disabilities (p≥0.05). Conclusion. It can be concluded that exercise training with Thera- Band for 6 weeks cannot improve CRF and upper limb disabilities in breast cancer survivors. Future studies with large sample size and long period of intervention is suggested.

KEY WORDS Exercise, Cancer, Fatigue, Upper Limb Function
INTRODUCTION

Cancer-related fatigue (CRF) is a common side effect in the all types of cancer treatment [1]. It has been reported that 70 to 100 percent of cancer patients will experience CRF from the time of diagnosis [2]. Physiological, biochemical, psychological and behavioral factors contribute to CRF. Indeed, a variety of symptoms included anxiety, pain, sleep disruption and altered body image is associated with CRF in breast cancer survivors [3]. CRF differs from other types of fatigue in that it is totally not refine by sleep or rest [4]. It seems that CRF can impair the activities of daily living in breast cancer survivors [5]. Also, it has been approved that CRF will reduce the adherence to breast cancer treatment [6]. Although some symptoms can improve following treatment completion, but fatigue persists in a number of breast cancer patients. On the other hand, 19-38% of patients experience significant levels of fatigue following treatment, and in some cases, fatigue continues for years after the ended of breast cancer treatment[6,7]. In breast cancer survivors, CRF persist during and after therapeutic treatment and they will experience CRF for months or years after successful treatment [8]. Bower et al (2006) reported that approximately 33% of patients with breast cancer will have persistent fatigue up to ten years into survivorship [9]. Also, it has been approved that CRF might be considered a strong predictor of lower survival in cancer patients [10]. Therefore, CRF included “a distressing, persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not refined by rest or sleep [11]. Indeed, CRF has a negative impact on Quality of life (QoL) and other cancer-related symptoms, such as pain, depression, and nausea [12]. It seems that breast cancer survivors suffer from CRF during and after treatment period and it resulting in low QoL and poor activities of daily livings.

The upper limb disabilities are common phenomena in breast cancer and asses by disabilities in arm, shoulder and hands (DASH) questionnaire. It expresses the functional performance of upper limb during activities daily livings in cancer survivors. Also, there is a relationship between upper limb impairments and quality of life in breast cancer survivors. [13]. It seems that pain can affect the upper limb function in breast cancer patients. Pain is a common problem in cancer patients; 45-59 percent of cancer survivors report that they suffer from pain. Also, pain is a subjective, multifactorial and complex symptom, resulting from the interaction between cognitive, sensory, emotional, cultural aspects, and previous experiences [14]. Some mechanisms have been suggested for upper limb disabilities in breast cancer patients included surgery, radiation therapy and chemotherapy. For instance, most common pain syndrome resulting from chemotherapy is chemotherapy-induced peripheral neuropathy (CIPN) [15]. Risk factors for CIPN are pre-existing neuropathies, older age and genetic polymorphisms [16]. In general, it has been found that breast mastectomy can increase the pain and DASH in breast cancer survivors [17]. Also, after the treatment, DASH can change the QoL in patients with breast cancer [14]. However, it seems that upper limbs disabilities is one the most important complexity in patients with breast cancer and it can have negative effects on QOL and CRF.

Recently, physical and exercise training has been recognized as a key factor of treatment and rehabilitation for many chronic diseases,
such as cancer. Some evidence shows that physical activity or exercise training may reduce the risk of breast cancer induced death [18]. McNeely et al (2006) found that exercise training is effective intervention to improve quality of life, cardiorespiratory fitness, physical functioning and fatigue in patients with breast cancer [19]. Also, Rahnama et al (2010) demonstrated that combination (aerobic and resistance) exercise training improve aerobic capacity in breast cancer survivors [20]. Indeed, Komer et al (2013) reported that increased physical activity levels and exercise after week 1 and throughout rehabilitation is possible and safe in the early period of cancer rehabilitation [21]. On the other hand, most of researchers use predominantly aerobic exercise to improve the CRF or pain in breast cancer survivors. For instance, a study found that supervised aerobic exercise can reduces CRF in breast cancer survivors [22]. However, resistance training recommend to patients with breast cancer. In a systemic review, De Backer (2009) concluded that resistance training is well-tolerated in cancer patients and it is good tool to reduce side effects of cancer and its treatment [23]. A new method of exercise training is resistance exercise with Thera-Band. Exercise with Thera-Band is recommended to special population, such as breast cancer survivors. The Thera-Band made from elastic materials and has been designed in different colors types that indicate resistance levels. For example, the yellow and red bands show lower and higher resistance, respectively. Thera-band can be applied to strenuous exercises tailored to the levels of functioning in special population [24]. Pourtaghi et al (2017) demonstrated that exercise with Thera-Band could increase muscular strength and improve quality of life in the older adults [24]. Although resistance training has some positive effects for breast cancer survivors, but effect of resistance training with Thera – Band on CRF and upper limb disabilities is not clear. Also, Until today, we found any study that indicates the effects of exercise with Thera-Band on fatigue and upper limb disabilities in breast cancer survivors. Thus, the aim of current study is to evaluate the effect of 6 weeks exercise with Thera-Band on CRF and upper limb disabilities in breast cancer survivors.

METHODS

Subjects. After surveying the 1200 files of patients with breast cancer and then telephone interviews, 320 patients were ready to participate in this study. Finally, 50 women aged 29-65 years as inclusion criteria included: 1) female, age range 29 to 65 years, 2) with the diagnosis of breast cancer, a stage of 0-III 3) have undergone breast surgery for at least twelve months 4) have a completed radiotherapy and chemotherapy 5) no new history of upper and lower body rehabilitation (six months before breast cancer diagnosis) 6) no regular exercise practice or less than two training sessions per week, in the last six months and 7) removal of the lymph nodes, were divided in to two groups: resistance with Thera-band group (n=25) and control group (n=25). In the post-test, 8 patients in the resistance with Thera-band group and 4 patients in control group were excluded, respectively. All subjects were completed inform constant and demographic data forms.

Exercise with Thera-Band Program. The progressive and supervised resistance training program was designed as ACSM prescription guidelines for 6 weeks [25]. Before starting the exercise program, the subjects were asked to choose their appropriate Thera – Band (red and then green color) in the first session of first week of training. After 5 minutes warm up, 9 resistance training (bench press, seated rowing, leg extension, shoulder press, leg press, thigh abduction, arm curl, arm
extension and thigh adduction), were done with Thera – Band in exercise training group. Each subject were performed these exercise 8 to 12 repetitions and 2 sets in the first two weeks. For overload principle, the were performed 8 to 12 repetitions and 3 sets in the second two weeks and 8 to 12 repetitions and 4 sets in the third two weeks [26,27]. The rest between each set was started from 90 seconds in the first week and was decreased to 45 seconds in the sixth week (detail in table 1). The rest between each move was gradually decreased from 3 minutes in the first week to 1 minute in the last week. To ensure about the enough rest and recovery between training sessions, subjects did not participate more than 3 sessions per week. In order to increase the workout intensity, Thera - Band length was changed. All subjects in exercise group were performed the resistance training with Thera – Band for six weeks. Control group subjects were followed usual care that recommended by the physicians in relation to healthy lifestyle. Also, control group subjects were not participated in any supervised exercise training but they have permission to do any activities that done before participation to this study.

Questionnaire. For CRF, the Piper Fatigue Scale was used. The Piper Fatigue Scale is the measurement tool for assessing the CRF. This questionnaire has 22 numerical items that measurement the fatigue experienced by the survivors. Therefore, Piper Fatigue Scale by using a 0–10 numerical scale, measures 4 dimensions of subjective fatigue: behavioral/severity, affective meaning, sensory and cognitive/mood. The total fatigue score is calculated by adding the 4 subscale scores and dividing by 4 [28]. This questionnaire was completed in pretest, at the beginning of the program, and 24 hours after last session of exercise with Thera-Band in resistance training with Thera band Group. Also, control group subjects were completed the questionnaire in pre-test and 6 weeks later.

For disabilities in upper limbs, DASH questionnaire was used. This questionnaire asks about symptoms as well as ability to perform certain activities in breast cancer survivors. The DASH includes of a 30-items, self-report questionnaire. Each item responses have 5 sections consist 1 (no difficulty), 2 (mild difficulty), 3 (moderate difficulty), 4 (sever difficulty) and 5 (unable). DASH SCORE = ([(sum of responses / n) - 1] x 25, where n is the number of uncompleted responses. If in a subject acquired questionnaire, there are greater than 3 missing items, DASH score may not be calculated.

Statistical analysis. Data were described as mean (M) and standard deviation (SD). Normal distribution was tested using the Kolmogorow-Smirnow test with Lilliefors correction demonstrating normality for the majority of the analyzed samples. Group effects (EXP vs. CON) and time effects (pre-test vs. post-test), as well as interaction effects (group x time) were calculated using a 2-way ANOVA (IBM SPSS V.20, Armonk, VA, USA: GLM, repeated measures). Significance was set at the 5% level (p≤.05).

**STATISTICAL RESULTS**
The characteristics of subjects and statistical analysis of data have been indicated in table 2 and table 3, respectively. We found a significant group effect between exercise with Thera - Band and control groups in the CRF ‘cognitive/mood’ dimension (p=0.034), and there were significant time effects for the CRF ‘affective meaning’ dimension (p=0.001) as well as for the CRF total score (p=0.049), but there were no significant interaction effects (Table 3). Thus, there was no treatment depending pre-post differences demonstrating any significant effect of 6
weeks resistance training with Thera-Band on CRF dimensions or DASH scores in breast cancer survivors in present study. However, ‘behavioral/severity’ (20%), ‘affective meaning’ (39%), ‘sensory’ (44%), and ‘cognitive/mood’ (26%) CRF scores decreased noticeably after resistance training with Thera–Band group. For the control group, there were no changes within the CRF dimensions ‘behavioral/severity’ and ‘sensory’, while the score for the CRF dimension ‘affective meaning’ decreased by 14%, and the score for the CRF dimension ‘cognitive/mood’ increased by 19%. The CRF total score decreased by 34% and 6% in the exercise with Thera–Band and control groups, respectively. Furthermore, the DASH total score increased by 17% and 3% in the exercise with Thera–Band and control groups, respectively.

| Table 1. Progression in resistance training with Thera–Band |
|-----------------------------------------------------------|
| Increasing the resistance | First and second weeks | Third and fourth weeks | Fifth and sixth weeks |
| Thera–Band Color | Training starts with selected color (red or Green) |
| Thera–Band Length | When using any new color, start with an easy length and progressively up to the very strictly based on a Omni Scale |
| Repetitions | 8 | 10 | 12 |
| Rating of Perceived Exertion | 3-5 | 6-9 | 10-12 |
| Sets | 2 | 3 | 4 |
| Rest between Sets (seconds) | 90 | 60 | 45 |
| Rest between each movements (minutes) | 3 | 2:30 | 2 |

| Table 2. Sample characteristics in Exercise (EXP) and the Control (CON) groups (M ±SD) |
|-----------------------------------------------|
| Age (years) | Weight (kg) | BMI (kg.m⁻²) |
| EXP | 46 ± 5.8 | 71.9 ± 5.8 | 25.7 ± 3.9 |
| CON | 46 ± 7.2 | 70.5 ±8.1 | 25.2 ± 3.7 |
Table 3. Descriptive statistics and group, time, and interaction effects of a 2-way ANOVA for the EXP and CON groups

|                          | Descriptives M (SD) | ANOVA factors: F (P) |
|--------------------------|---------------------|----------------------|
|                          | Pre                 | Post                 | Group | Time | Group x Time |
| behavioral/severity score| EXP 2.9± 2.3        | 2.3 ± 2.1            | 0.660 | (0.42) | 0.85 (0.36) | 0.85 (0.36) |
|                          | CON 3.1 ± 2.3       | 3.1 ± 2.3            |       |      |             |             |
| affective meaning score  | EXP 2.8 ± 2.3       | 1.7 ± 1.5            | 3.145 | (0.08) | 12.84 (0.001)* | 0.71 (0.4) |
|                          | CON 4.7 ± 0.2       | 4.0 ± 0.5            |       |      |             |             |
| sensory score            | EXP 3.6 ± 2.5       | 2.0 ± 1.2            | 0.866 | (0.35) | 2.51 (0.12) | 3.13 (0.08) |
|                          | CON 3.5 ± 0.6       | 3.5 ± 2.6            |       |      |             |             |
| cognitive/mood score     | EXP 2.3 ± 1.2       | 1.7 ± 1.6            | 4.856 | (0.03)* | 0.01 (0.91) | 3.77 (0.06) |
|                          | CON 3.2 ± 2.4       | 3.8 ± 2.8            |       |      |             |             |
| CRF total score          | EXP 2.9 ± 2.6       | 1.9 ± 1.6            | 2.52 | (0.12) | 4.13(0.04)* | 1.35 (0.25) |
|                          | CON 3.6 ± 2.4       | 3.4 ± 2.3            |       |      |             |             |
| DASH total score         | EXP 327.0± 79.0     | 383.8±88.5           | 0.22  | (0.63) | 0.53 (0.46) | 0.25 (0.619) |
|                          | CON 375.0±147.5     | 385.6±186            |       |      |             |             |

DISCUSSION

The current study assessed the effect of 6 weeks resistance training with Thera – Band on CRF and upper limb disabilities in breast cancer survivors. The present study found that 6 weeks resistance training with Thera - Band has no positive effects on CRF in women with breast cancer (p˃0.05). However, CRF was reduced in resistance training with Thera – Band group 34 percent. In contrast with this study, some authors reveled that resistance training has positive benefits for CRF in breast cancer survivors. For instance, Milne et al (2008) reported that combined aerobic and resistance training 3 times a week for 12 weeks reduce CRF and improve muscular strength in breast cancer patients [29]. Also, Cantarero-Villanueva et al (2011) found that 8 weeks supervised multimodal exercise program and multimedia support reduce CRF in breast cancer survivors [30]. Brown et al (2011) mentioned that exercise interventions for more than 28 weeks, nearly 3 sessions per week and lasting 40 minutes per session have positive effects for CRF [31]. A main different between current study and previous studies was the short period...
and different types of resistance training equipment (Thera – Band). However, previous studies were used common resistance training for long period. Also, a randomized controlled trial indicated that exercises and recovery strategies (massage immediately after the exercise training program), following a body-mind approach, more effectiveness than when used alone [32]. Meneses-Echávez et al (2015) reported that high volume exercise training is safe and appropriate for breast cancer survivors and it can reduce CRF in this patient [22]. In present study, short period of intervention with new equipment, Thera – Band, was used as intervention. It seems that period of intervention was not enough to change the CRF in breast cancer patients.

Some mechanisms have been suggested for CRF. One hypothesis is that cancer and cancer treatment can increase the brain serotonin (5-HT) concentration and its receptor in postsynaptic space. It has been established that 5-HT has an important role in central fatigue [33]. In addition, pro-inflammatory cytokines such as, tumor necrosis factor (TNF)-α, interleukin (IL)-1β, interferon (IFN)-α, IFN-γ, can stimulate Indoleamine 2,3-dioxygenase to alter 5-HT metabolism that resulting to central fatigue [34]. Another possible mechanism is related to circadian rhythm disruption. In cancer patients, endocrine rhythm, metabolic process and immune function and can alter and resulting in CRF. For instance, breast cancer and its treatments can result in muscle metabolism disruption that lead to CRF [35]. Indeed, comorbidities included anemia, sleep disorder, depression and cachexia can increase the risk of CRF [5]. It seems that 6 weeks resistance training with Thera- Band has no positive effects on these variables and therefore it cannot change the CRF in cancer survivors. However, these mechanisms and its relationship with resistance training in breast cancer patients should be approve by future studies.

Another important finding of current study was that 6 weeks resistance training with Thera – Band had no significant effect on upper limb disabilities in breast cancer survivors. In contrast with present study finding, Sener et al (2017) urged that clinical Pilates exercises can improve the upper extremity function after breast cancer treatment [36]. It seems that the insignificant effect of resistance training with Thera – Band on DASH is related to type II error, statistically. In present study, short period of intervention (6 weeks) was used. Also, sample size in current study was small. Therefore, it has been suggested that future studies run with large sample size for long period with Thera – Band in these patients.

The current study had several strengths. This study was done with new equipment for training, Thera – Band. Also, supervised training was selected as intervention for breast cancer survivors. Indeed, present study had several limitations included small sample size, short period of intervention, no control on social and mental behavior.

To our knowledge, this is the first study including the effects of resistance training with Thera – Band on CRF and DASH in breast cancer survivors. The future studies should focus on long period intervention with large sample size. Also, some mechanisms that involve in CRF and DASH such as pro-inflammatory cytokines, some hormones (Cortisol and 5-HT), circadian rhythms and ATP metabolism should be considered.

Conclusion. In conclusion, it was found that 6 weeks resistance training with Thera-Band cannot improve CRF and upper limb disabilities in breast cancer survivors. Future studies with large sample size and long period of intervention with Thera – Band are suggested.
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