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The Effects of Resistance Training on Fatigue during Chemotherapy for Patients with Breast Cancer

Bachelor's thesis in Human Movement Science
Supervisor: Xiao-Mei Mai
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Abstract

Background: Breast cancer is the most commonly diagnosed cancer worldwide, accounting for 12.5% of all new annual cases. Most of these patients will have to undergo chemotherapy as a treatment method and will, consequently, suffer from side effects during and/or after finished treatment. Despite the high prevalence of complications experienced by breast cancer patients, there is limited research conducted on how to prevent or limit them. When looking into the effect of resistance training on fatigue as a side effect of chemotherapy, there is insufficient research. The aim of this literature review study is to investigate if resistance training has any effect on reduction of fatigue for breast cancer patients undergoing chemotherapy. **Methods:** The systematic literature search was conducted using the PubMed database. Relevant literature was identified using search criteria including patients with breast cancer undergoing chemotherapy, resistance training program and measured fatigue. The included studies had to be randomized controlled trials or clinical trials. **Results:** Eight original papers were included in this literature study. Seven out of eight studies found an indication that exercise, including resistance training, had a significant effect on cancer-related fatigue. **Conclusion:** This literature review study suggested that the effect of resistance training on reduction of fatigue among patients with breast cancer undergoing chemotherapy was promising.

Abstrakt

Bakgrunn: Brystkreft er den mest diagnostiserte kreftformen på verdensbasis, og står for 12,5 % av alle nye årlige tilfeller. De fleste av disse pasientene vil måtte gjennomgå cellegift som behandlingsmåte og vil oppleve vonde bivirkninger under og/eller etter avsluttet behandling. Til tross for den høye forekomsten av komplikasjoner som brystkreftpasienter opplever, er det begrenset forskning utført på hvordan man kan forebygge eller begrense dem. Når man skal undersøke effekten av styrketrening på fatigue som en bivirkning av cellegift, finnes det ikke tilstrekkelig forskning. Målet med denne litteraturstudien er å undersøke om styrketrening har noen effekt på reduksjon av fatigue for brystkreftpasienter som gjennomgår cellegiftbehandling. **Metode**: Det systematiske litteratursøket ble utført ved bruk av databasen til PubMed. Relevant litteratur ble identifisert ved hjelp av søkekriterier som inkluderte pasienter med brystkreft som gjennomgikk cellegiftbehandling, styrketreningsprogram og målt fatigue. Forskningsdesignet måtte være randomiserte kontrollerte studier eller kliniske studier. **Resultater**: Åtte originalartikler ble inkludert i denne litteraturstudien. Syv av åtte studier fant en indikasjon på at trening som inkluderer styrketrening hadde en signifikant effekt på kreftrelatert fatigue. **Konklusjon**: Denne litteraturstudien antydet at effekten av styrketrening på reduksjon av fatigue blant pasienter med brystkreft som gjennomgikk cellegift var lovende.

Keywords: Breast cancer, Chemotherapy, Cancer-related fatigue, Resistance training.

Introduction

Breast cancer (BC) is one of the most prevalent types of cancer with approximately 2.3 million women worldwide being diagnosed in 2020 (*Breast Cancer Statistics And Resources | Breast Cancer Research Foundation | BCRF*, 2021). Chemotherapy (CT) is a commonly used treatment method for BC that uses drugs to kill cancer cells. The amount and frequency of CT varies between patients and regularly lasts for 3-6 months (*Chemotherapy for Breast Cancer | Breast Cancer Treatment*, no date). This form of cancer treatment does not exclusively kill fast-growing cancer cells and therefore also affects the growth of healthy cells in the patient. This is the main cause of common side effects such as pain, anemia, fatigue and more. Since CT can be physically and mentally draining, it is given in cycles which range from two to three weeks. This way, the body has time to recoup before the next dosage of CT is scheduled.

One of the most common and impairing side effects of CT is cancer-related fatigue, which can be defined as a "*persistent, subjective sense of tiredness related to cancer and cancer treatment that interferes with usual functioning*" (Bower *et al.*, 2000). Cancer-related fatigue interferes with daily life activities and has significant consequences for the patients quality of life (QoL) during and after cancer treatment. The prevalence of cancer-related fatigue for those with ongoing treatment varies between 62-85%, whereas 9-45% reported moderate to severe cases (Thong *et al.*, 2020). Cancer-related fatigue can last for months, or even years, after the completion of cancer treatment and as life expectancy increases so does the significance of side-effects (Andrykowski, Curran and Lightner, 1998). As fatigue is subjective, the most common way to measure it is by using self-reporting questionnaires (Thong *et al.*, 2020). These questionnaires can either be uni- or multidimensional. A unidimensional questionnaire is designed to exclusively look at one dimension of fatigue, for example *general* fatigue or *physical* fatigue. Contrary, a multidimensional questionnaire includes several classifications of fatigue such as total, physical, affective and cognitive. Although these questionnaires help estimate levels of fatigue, it is still difficult to pinpoint exact statistics. This leads to cancer-related fatigue being undertreated and underdiagnosed (Thong *et al.*, 2020).

According to the World Health Organization, physical activity (PA) is “any bodily movement produced by skeletal muscles that require energy expenditure” (*Physical activity*, no date). PA includes all forms of exercise, both anaerobic and aerobic, and leads to improvements in muscular fitness, cardiorespiratory fitness and bone and functional health. For cancer patients undergoing CT, PA is recommended by The American College of Sports Medicine (ACSM) as it is proven to increase physical function and health-related QoL as well as decreasing side-effects, such as fatigue and depression (Gebruers *et al.*, 2019). However, there is no specific guideline as to which type or the amount of exercise that is most efficient. Resistance training (RT) refers to any form of PA that forces the muscles to contract by exercising against an external resistance. The external resistance can be dumbbells, barbells, weight machines, resistance bands, bodyweight or any other object that creates muscle contraction. The aim of RT is to build muscular strength, anaerobic endurance and/or size of skeletal muscles.

Regular exercise programs have been proven to improve the physiological health, disease, treatment-related side effects, and QoL in women treated for BC (Cormie *et al.*, 2017). Furthermore, in a study conducted by Van Vulpen et al. it is shown that physical exercise during BC treatment has beneficial effects with lower levels of fatigue (van Vulpen *et al.*, 2016). Excluding fatigue, other benefits of RT for BC patients are similar to those among the general population; an increase in muscle strength, endurance and bone mass, as well as a greater ability to perform activities of daily living. These benefits from RT are critical to BC patients for maintaining the ability to perform activities of daily living, controlling body weight, participating in PA and returning to life after treatment (Lite and Mejia, 2010).

Despite the aforementioned benefits, there is still a research gap on the relationship between RT and fatigue among patients under CT treatment. The purpose of this literature review study is to evaluate the possible effect of RT on reducing fatigue during CT for patients with BC.

Methods

Literature search and selection criteria

A systematic literature search was performed using the PubMed database. Following keywords were used "Resistance training" AND "fatigue" AND "Chemotherapy" AND "Breast Cancer". The initial search provided a result of nineteen original articles of interest. To fit the scope of our research question more appropriately, the inclusion criteria were modified using the filter function on PubMed where all the studies had to be either randomized controlled trials (RCT) or clinical trials and conducted on humans. The articles had to be published in English and conducted on patients with breast cancer undergoing chemotherapy while following a resistance training program, as well as measuring cancer-related fatigue. The articles that did not satisfy the inclusion criteria were excluded and resulted in the total of eight relevant studies analyzed in this literature study. The main characteristics of the selected studies are described in Table 1. The studies are listed following a sequence of publication years, from oldest to newest.

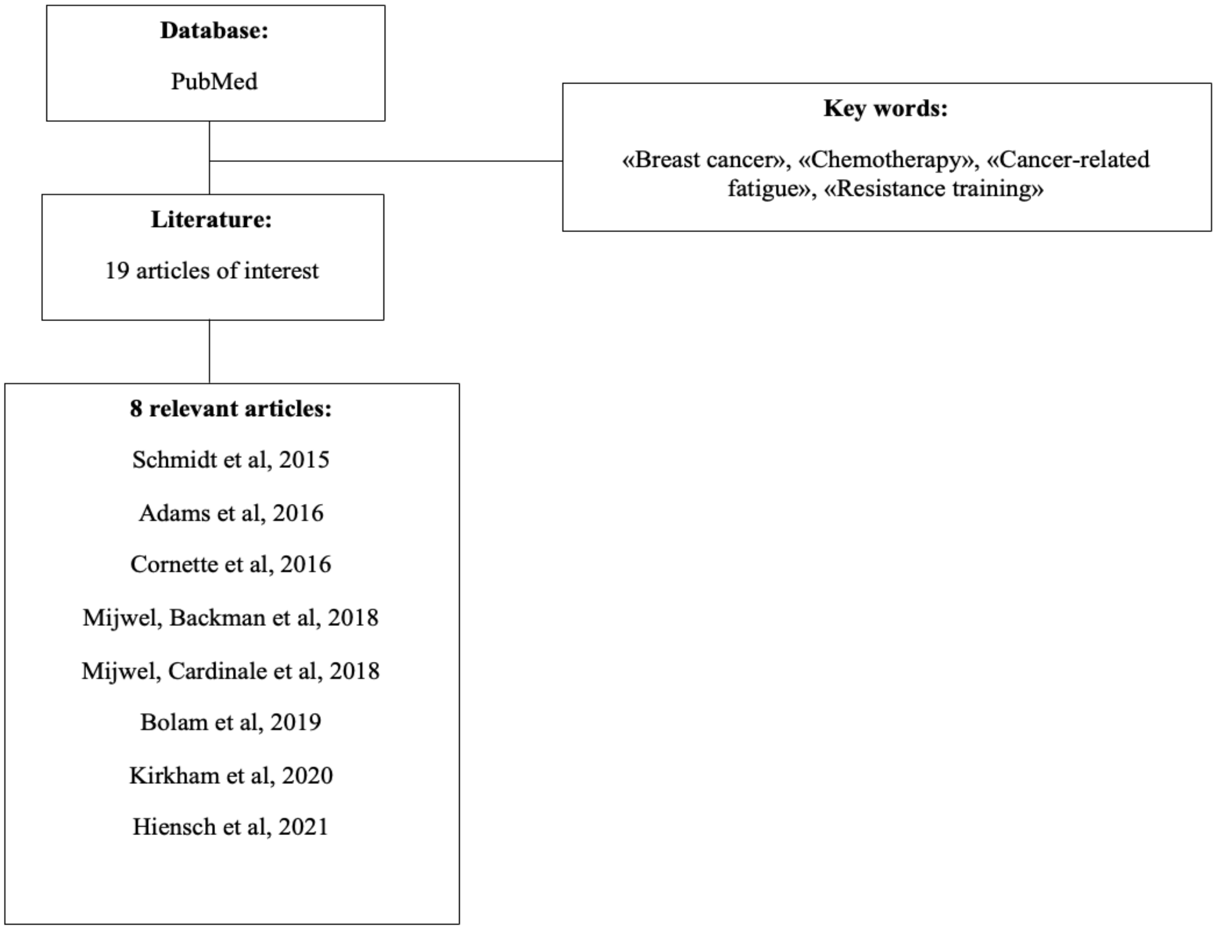

Figure 1: Flow chart of the literature search on whether resistance training has an effect on fatigue during chemotherapy for patients with breast cancer.

Results

Eight studies investigated the effect of RT on reducing fatigue in BC patients undergoing CT. Six of the studies showed an exclusive decrease in fatigue, one showed both decrease and no significant change while one found no significant change. In the five studies that evaluated aerobic training separately, four showed no significant change while one showed a decrease in fatigue. Seven of the studies based the change in fatigue on the usual care (UC) group in order to compare and identify an increase or decrease in fatigue. *Schmidt et al. (2015)* used a relaxation group instead of UC. Table 1 presents an overview of the characteristics of the original articles. Further, the findings in each of the articles will be described in more detail.

Table 1: Characteristics of the original studies

Author, year	**Study design**	**Population and sample size (n)**	**Exercise type, frequency**	**Duration**	**Results**
Schmidt et al, 2015	RCT	Total (n): 95 RT (n): 49 Relaxation group (n): 46	Supervised assisted RT program 2x / week	12 weeks	**RT**:↓ Fatigue **Relaxation group:** ⇔ Fatigue
Adams et al, 2016	RCT	Total (n): 200 AT (n): 64 RT (n): 66 UC (n): 70	Supervised RT Supervised AT 3x / week	17 weeks	**RT**: ↓ Fatigue **AT**:⇔ Fatigue
Cornette et al, 2016	RCT	Total (n): 42 APA (n): 20 UC (n): 22	Home based strength and aerobic training RT: 1x per week Aerobic: 2x per week	54 weeks	**APA:** ⇔ Fatigue
Mijwel, Backman, et al, 2018	RCT	Total (n): 206 RT-HIIT (n): 74 AT-HIIT (n): 72 UC (n): 60	RT-HIIT AT-HIIT 2x / week	16 weeks	**RT-HIIT:** ↓ Fatigue & ⇔ Fatigue **AT-HIIT:** ⇔ Fatigue
Mijwel, Cardinale, et al, 2018	RCT	Total (n): 23 RT-HIIT (n): 7 AT-HIIT (n): 6 UC: 10	RT-HIIT AT-HIIT UC 2x / week	16 weeks	**RT-HIIT:** ↓ Fatigue **AT-HIIT:** ↓ Fatigue
Bolam et al, 2019	Clinical trial	Total (n): 160 RT-HIIT (n): 58 AT-HIIT (n): 54 UC (n): 48	RT-HIIT AT-HIIT UC 2x / week	16 weeks	**RT-HIIT:** ↓ Fatigue **AT-HIIT**: ⇔ Fatigue
Kirkham et al, 2020	RCT	Total (n): 27 Exercise group (n): 12 UC (n): 15	Supervised aerobic and RT program 3x / week	8-12 weeks	**Exercise group:** ↓ Fatigue
Hiensch et al, 2021	RCT	Total (n): 86 RT-HIIT (n): 30 AT-HIIT (n): 27 UC (n): 29	RT-HIIT AT-HIIT UC 2x / week	16 weeks	**RT-HIIT**: ↓ Fatigue **AT-HIIT**: ⇔ Fatigue

↑ **= Increase;** ↓ = Decrease; ⇔ = No change; AT = Aerobic Training; RT = Resistance Training; UC = Usual Care; APA = Home-based adapted physical activity; RT-HIIT = Resistance Training High Intensity Intervals; AT-HIIT = Aerobic Training High Intensity Intervals

(Schmidt *et al.*, 2015) conducted a randomized controlled intervention trial comparing a 12-week supervised progressive RT program to a supervised group-based progressive relaxation training program. The study population consisted of 95 early stage BC patients (52.7 ± 10 years) undergoing adjuvant CT. Its primary result was cancer-related fatigue, while its secondary outcomes involved CT induced side effects which include QoL, depression, and cognitive capacity. Both the RT group (n = 49, 52.2 ± 9.9) and relaxation group (n = 46, 53.3 ± 10.2) were supervised and performed their interventions approximately 60 minutes twice a week for 12 weeks. Exercise was implemented with the use of machine based RT and included eight exercises which covered the major upper and lower muscle groups. The relaxation group used a relaxation method that did not include any form of aerobic or RT. Cancer-related fatigue was determined by using the Fatigue Assessment Questionnaire (FAQ) which is a 20-item, multidimensional self-assessment questionnaire. The results of the study concluded that RT appeared to mitigate physical fatigue while maintaining QoL and reducing CT induced side effects. The relaxation group showed fatigue and social function to be worsened during CT.

(Adams *et al.*, 2016) examined the effects of RT and aerobic training on sarcopenia, dynapenia, and QoL changes in early stage BC patients receiving CT. By focusing on sarcopenia and dynapenia, the study explored fatigue as being associated with loss of muscle mass. A total of 200 patients (48.8 mean age, range 25-78 years) participated and were randomized into groups of UC (n=70), RT (n=66) and aerobic training (n=64). Participants in the RT and aerobic training groups were asked to perform their prescribed exercises three times per week throughout the duration of their CT treatment. Both groups were supervised during their exercise sessions. The RT group performed two sets of 8-12 repetitions of nine exercises between 60-70% of their one repetition maximum. The aerobic training group were prescribed 60 minutes of either treadmill, cycle ergometer or elliptical based exercise. The UC group were asked to not participate in any new exercise programs during the course of their treatment. All participants were asked to use the Functional Assessment of Cancer Therapy-Anemia (FACT-An) scales, including the Trial Outcome Index-Anemia (TOI-An) subscale for fatigue. In the conclusion of their study, RT significantly reversed sarcopenia and showed reduction in dynapenia while consistently demonstrating superior effects to the UC group for improving sarcopenia-related outcomes.

Consequently, as preventing or limiting sarcopenia is associated with clinically and statistically significant differences in fatigue, their findings within limiting sarcopenia resulted in reduction of fatigue in the RT group.

(Cornette *et al.*, 2016) conducted a RCT exploring the effects of home-based exercise training on rate of oxygen (VO2) as well as cancer-related fatigue in BC patients under adjuvant or neoadjuvant CT, followed by radiotherapy. A total of 42 early stage BC patients (50.5 mean age, range 37-73 years) treated with CT participated in the study. The participants were divided into two groups: APA group (n=20) and a UC group (n=22). The APA group combined RT and aerobic training. RT was implemented once per week and included exercises for five muscle groups performed with two sets of 8-12 repetitions. Aerobic training consisted of cycling on an ergometer cycle twice a week or walking outside with an intensity that was individualized based on heart rate and power. The UC group was encouraged to remain their regular PA level during and after CT and radiotherapy treatment. Exercise adherence was assessed by a heart rate monitor watch and exercise diaries. Results showed a 109% aerobic training adherence and 46% RT adherence. Fatigue was assessed with the Multidimensional Fatigue Inventory (MFI-20). The participants completed the questionnaires prior to CT (T0), 27 weeks after baseline and the end of CT (T1), and 27 weeks after completing the CT treatments (T2). The study observed no difference in fatigue between the two groups at T1 and T2, nor before or after treatment.

(Mijwel, Backman, *et al.*, 2018) examined physiological responses to concurrent resistance and high-intensity interval training during CT in an RCT called OptiTrain (Optimal Training for Women with Breast Cancer) for 16 weeks. The OptiTrain study investigated the effect of different exercise regimens on cancer-related fatigue as the primary outcome. This study distributed 206 female early stage BC patients into three different groups: RT-HIIT (n=74, 52.7±10.3 years), AT-HIIT (n=72, 54.4±10.3 years) and UC (n=60, 52.6±10.2 years). The RT-HIIT group performed two to three sets of 8-12 repetitions at an intensity of 80% of their individual estimated one-repetition maximum, with progressive overload being ensured. RT-HIIT included exercises using bodyweight, dumbbells or barbells. The AT-HIIT group performed 20 minutes of moderate-intensity aerobic exercise (rating of perceived exertion of 13-15 on the Borg scale) with the use of a cycle ergometer, elliptical ergometer or treadmill. Lastly, both exercise groups concluded each session with 3x3 minute bursts of HIIT (rate of perceived exhaustion 16-18) with one minute of recovery. The exercise groups trained twice a week and all sessions were supervised. Cancer-related fatigue was measured by the unidimensional European Organization for Research and Treatment for Cancer Quality of Life Questionnaire (EORTC QLQ-C30) and the multidimensional Piper Fatigue Scale (PFS). The UC group reported an increase of cancer-related fatigue measured by the EORTC QLQ-C30 during the study, while the RT-HIIT and AT-HIIT reported no change. However, the RT-HIIT group showed a decrease in cancer-related fatigue in the results assessed with the PFS while the UC group reported increased levels. The AT-HIIT group showed no change in self-reported fatigue scores.

(Mijwel, Cardinale, *et al.*, 2018) investigated the relationship between markers of skeletal muscle function and different exercise regimens. Amongst other factors, muscle strength, mitochondrial content and cancer-related fatigue were examined in 23 participants obtained from the Optitrain RCT. The study included a random distribution of female early stage BC patients receiving CT while participating in either RT-HIIT (n=7, 54.3±11 years), AT-HIIT (n=6, 51.5±7 years) or UC (n=10, 51±13 years) for 16 weeks. The protocol for the Optitrain exercise training intervention has been previously described. Mitochondrial content was presented by muscle citrate synthase activity and assessed by analyzed muscle tissue samples, extracted from M. vastus lateralis by needle biopsy. Muscle strength was determined by an isometric midthigh pull and cancer-related fatigue was self-assessed by the EORTC QLQ-C30 questionnaire. All data was collected both pre- and post intervention. The results showed a significant reduction in muscle citrate synthase activity in the UC group compared to both the RT-HIIT group and the AT-HIIT group (UC vs. AT-HIIT, P=0,005; UC vs. RT-HIIT, P=0,0027). A significant association between change in muscle citrate synthase activity and change in fatigue was found. Furthermore, an association between muscular strength in the lower extremities and muscle citrate synthase activity was also present. The study referred to the Optitrain RCT data for the results of the EORTC QLQ-C30 questionnaire, where an increase in fatigue in the UC group was found in contrast to the exercise groups, who both had a decrease in fatigue levels. The exercise groups displayed either stable or increased levels of skeletal muscle function markers, whereas the UC group reported reduced levels.

(Bolam *et al.*, 2019) conducted a two-year follow-up study of the 16-week OptiTrain RCT. This study investigated whether any alterations had occurred in cancer-related fatigue, as well as QoL, muscle strength, PA levels and other health-related outcomes between the two OptiTrain exercise groups and UC group, two years post-baseline. A population of 179 women diagnosed with early stage BC were qualified and approached for the follow-up, and a total of 160 participants completed the assessments. The participants were randomly assigned to one of three groups; RT-HIIT (n=58, 53.4±10.1 years), AT-HIIT (n=54, 53.9±9.2 years) or UC (n=48, 54.1±9.6 years). Cancer-related fatigue was assessed by the Swedish version of the revised PFS. The results showed that the RT-HIIT group reported statistically significant positive differences both in cancer-related fatigue and lower limb muscle strength compared to the UC group at two years. The AT-HIIT group had no significant change in cancer-related fatigue.

(Kirkham *et al.*, 2020) examined the effect of CT-periodized exercise on cancer-related fatigue. The EXIT trial was a two-arm RCT where female early stage BC patients scheduled to receive taxane-based CT were randomly divided into either a CT-periodized exercise program (n=12, 51±8.1 years) or UC (n=15, 49.5±11 years). To evaluate exercise adherence during CT, a periodized exercise prescription in accordance with the treatment cycle length was compared to a standard linear progression prescription from NExT, a prior study conducted by the same research team with a similar population (n=51, 51.9 ±11.7 years). Participants in both studies were provided with three supervised aerobic and full body RT sessions per week as well as encouraged to complete two home based aerobic training sessions. Aerobic training was conducted on either treadmills, cycle ergometers or elliptical machines. RT included exercises with the use of resistance bands, dumbbells or resistance machines. To investigate cyclical variations, both fatigue and steady state exercise responses in both groups of the EXIT study were evaluated prior to the first taxane treatment and three additional times during the third cycle (i.e., 0-3 days prior, 3-5 days post third treatment, and 0-3 days prior to the fourth treatment). Fatigue was assessed by the total fatigue score from the revised PFS and exercise responses were determined by a submaximal steady state exercise test. The results indicated that the UC group reported higher levels of fatigue and a greater magnitude of fatigue fluctuations than the exercise group. The study also reported that the CT-periodized exercise prescription in EXIT showed higher overall attendance (78%±23%) during CT than the standard linear exercise prescription used in NExT (63%±25%, P=0.05).

(Hiensch *et al.*, 2021) conducted a RCT exploring whether the effects of exercise on fatigue were affected by changes in inflammation. The study population was drawn from the original Optitrain RCT, although only participants with a > 60% attendance to the exercise program were included together with a random sample of controls. Female early stage BC patients receiving CT were randomized to one of three groups; RT-HIIT (n=30, 52.2±10.1 years), AT-HIIT (n=27, 53.9±7.4) or UC (n=29, 52.9±10.1). The exercise protocols for RT-HIIT and AT-HIIT have been previously described in this literature study. Blood samples, physical measurements and questionnaires were collected at baseline (before randomization) and post intervention. Cancer-related fatigue was self-reported using the validated Swedish version of the PFS and inflammatory markers were assessed by analyzed plasma samples. This resulted in the assessment of 92 inflammatory markers (e.g., interleukin-6 [IL-6] and tumor necrosis factor α [TNF-α]). This study shows an overall increase in inflammation during CT for all groups. However, single inflammatory markers such as IL-6 and T-cell surface glycoprotein CD8 alpha chain (CD8a) were significantly less pronounced in the RT-HIIT group compared to the UC group after 16 weeks. No significant differences in single inflammatory markers were found in the AT-HIIT group compared to the UC group. The two inflammatory markers IL-6 and CD8a showed moderate positive effects of exercise on total and physical fatigue. This observation was only made in the RT-HIIT group.

Discussion

All of the eight selected studies investigated the relationship between RT and reduction of fatigue for BC patients undergoing CT. The studies all included a variation of RT, whereas seven consisted of a supervised form of RT at a facility while one relied on an unsupervised home based program. In addition, six of the studies included a combination of RT and aerobic training, while *Schmidt et al. (2015)* and *Adams et al. (2016)* differentiated between RT and aerobic training groups. Furthermore, seven of the studies used a UC group while *Schmidt et al. (2015)*

used a relaxation group. All of the studies used questionnaires as the main method of assessing fatigue.

Study design and sample size

Seven of the eight selected studies were RCT while one was a clinical trial. In this literary study, the sample size of the included studies varied from 23 to 206 participants, which is a considerable difference. Several selection biases might have occurred. For instance, in the studies conducted by *Mijwel, Backman, et al. (2018)* a relatively large number of participants in the UC group declined directly after randomization. In the study performed by *Hiensch et al. (2021)* they compromised their randomization by only admitting women with an attendance score higher than 60%. Consequently, these findings must be interpreted carefully as it is possible that the results were affected by the selection of participants with a fitness level not being fully representative for their study population. Lastly, there is a risk for dropouts in studies that involve BC patients undergoing CT treatment as death, recurrent cancer, change of treatment method or exhaustion from side effects is common.

Intervention time between studies

Four of the eight original articles had a study period of 16 weeks. The shortest study period lasted between 8-12 weeks, while the longest lasted 54 weeks. Only *Bolam et al. (2019)* had a follow-up period, of which lasted two years. In early stage BC, the duration of CT is approximately three to six months. The intervention time should accommodate for the full length of CT cycles in order to provide a clear understanding of its relationship with exercise (Hiensch *et al.*, 2021). However, it is challenging to conduct a study over a longer period when patients who undergo varying lengths, types and amounts of CT treatment are involved.

Exercise type

A clear limitation of this literary study is the variations of exercise programs prescribed and performed. Although the articles included a form of RT, six had the participants perform RT in combination with aerobic exercise while two exclusively prescribed RT. Furthermore, four of the original studies used RT-HIIT as an exercise type which is a combination of RT and aerobic endurance. Notably, in all of these studies fatigue was reduced for the RT-HIIT groups and only reduced in the AT-HIIT group in one of the studies. Although RT without the combination of aerobic endurance would give more clear evidence, as the three remaining studies showed no change in fatigue for the AT-HIIT group there is an indication that RT may be an influential factor. This theory is encouraged by the findings in *Schmidt et al. (2015)* and *Adams et al. (2016)* who examined RT exclusively and both found a decrease in fatigue in the exercise groups. *Adams et al. (2016)* suggested that RT is beneficial as it reduces loss of muscle mass and consequently reduces fatigue as well. Similarly, the four studies who obtained their participant data from the OptiTrain RCT also showed a significant reduction of fatigue in combination with increased lower limb muscle strength only in the RT-HIIT group. However, it is unclear if these results are caused exclusively by resistance- or aerobic training, or a combination of both. More studies which clearly distinguish between RT and aerobic training would be desirable to optimize future exercise prescriptions for treatment of CT-induced side effects such as fatigue.

Side effects and risks of chemotherapy

CT is a key source of fatigue, yet current knowledge regarding the effects of exercise during courses of treatment is limited. Increased levels of fatigue over the course of CT was observed in the control groups, in accordance with findings in several other studies (Schmidt *et al.*, 2015). The first week of a CT cycle is commonly the most intolerable, while the last week is the least strenuous. *Kirkham et al. (2020)* reported higher attendance during CT weeks for CT-periodized exercise group compared to the standard linear exercise prescription. Physical capacity and motivation to participate in exercise can therefore be exceedingly lowered for patients undergoing CT. The findings by *Kirkham et al. (2020)* emphasize that accommodation to CT cycles is beneficial for exercise adherence. Additionally, *Schmidt et al. (2015)* found a decrease in CT induced side effects in the RT group while *Adams et al. (2016)* showed that RT led to significant improvements in CT completion rate. These results highlight the promising effect of RT during CT.

Validity and reliability of measuring methods

A total of five different questionnaires were used to assess fatigue. The most common were EORTC-QLQ-C30 and the PFS. *Mijwel, Backman, et al. (2018)* used them both in combination. The remaining three studies used FAQ, FACT-An and MFI-20. Preferably, it would be beneficial to use less variation of questionnaires when looking for coherence across the studies. As seen in the study conducted by *Mijwel, Cardinale, et al. (2018),* their results differed between the questionnaires used. In the RT-HIIT group, no change in fatigue was reported using the unidimensional EORTC-QLQ-C30. In contrast, a decrease in fatigue was found for the same group when reporting through the multidimensional PFS. These findings may indicate that fatigue in BC patients is more accurately measured when using a multidimensional questionnaire which looks at several classifications of cancer-related fatigue instead of only one classification. Nevertheless, consistency of questionnaires across the studies would provide a more accurate foundation for comparison**.** Self-reporting questionnaires as an assessment method can prove to be a limitation as perception of fatigue can vary greatly between individuals. Some may have a higher tolerance for fatigue and consequently underreport their symptoms, while others might have a lower tolerance and therefore overreport their symptoms.

Divergence of fatigue outcomes

In contrast to the findings from the other studies, *Cornette et al. (2016)* and *Mijwel, Backman, et al. (2018)* found no change in cancer-related fatigue for the exercise groups. However, the latter study found a reduction of fatigue when using the PFS questionnaire in the same participant group. Dissimilar to the other articles, *Cornette et al. (2016)* included patients undergoing CT followed by radiotherapy and measured fatigue with the MFI-20 questionnaire. In addition, the study exclusively prescribed an unsupervised home-based exercise program. While the other articles had similar exercise adherence across RT and aerobic training, *Cornette et al.* (2016) reported remarkably higher exercise adherence for aerobic exercise in comparison to RT within the APA group. It is plausible that the difference in exercise adherence is caused by supervision and/or the simplicity of aerobic exercise in comparison to RT. Generally, the most preferable aerobic exercise type is walking (*CDC VitalSigns - More People Walk to Better Health*, 2013)**.** Walking was an alternative for aerobic exercise in the study conducted by Cornette *et al*. There is less experience and equipment needed in aerobic exercise while also being more accessible, making the threshold for completion lower. These factors could have influenced the results not being the same as the other seven studies as there is no supervision and more responsibility on the participants to complete the program themselves.

Future studies

More studies investigating long-term effects on how RT could counteract cancer-related fatigue would be beneficial to provide more evidence in regards to what kind of exercise strategies are most appropriate. Future studies should attempt to accommodate for treatment-related fluctuations in order to secure optimal exercise adherence and prescribe the most beneficial exercise program. Throughout conducting this literary study, it is evident that more research involving exclusively RT is needed when investigating its effect on BC patients undergoing CT.

Conclusion

This literature study included eight articles which addressed whether RT had a better effect on the reduction of fatigue for BC patients undergoing CT. Seven studies showed a reduction in fatigue, while two found no significant change in fatigue. After evaluating the strengths and weaknesses of the included studies, it is assumed that RT and combination of RT and aerobic exercise may result in a decrease in fatigue for patients with BC undergoing CT. As a consequence of the majority of the articles did not differentiate between aerobic training and RT while assessing fatigue, it is unclear whether the results are caused by RT alone or in combination with aerobic training. Therefore, it is necessary that future studies exclusively investigate RT as an exercise group to provide more evidence of reduction in fatigue.

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