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Effects and beneficial aspects of physical activity on cancer-related fatigue in the most common cancer types receiving chemotherapy: a literature review

BEV2900

Bachelor's project in Human Movement Science

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Kunnskap for en bedre verden

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Bachelor´s Thesis in Human Movement Science

BEV2900 – Spring 2021

Department of Neuromedicine and Movement Science, NTNU

Candidate number: 10029, 10039 & 10032

Number of words in abstract: 191 english, 187 norsk

Number of words in thesis: 4831

Abstract

Objective: Fatigue is a common effect during and after cancer treatment, and no gold standard for reducing fatigue is developed. This literature review will investigate the effect of physical activity on fatigue after chemotherapy in the most common cancer types (breast, prostate, lung and colorectal), and if there are any aspects of physical activity that are more beneficial. **Method:** PubMed, Google scholar and ScienceDirect were databases used to provide relevant articles for this literary review. **Results:** In total, nine studies were included. The main findings in this review indicates that physical activity appears to be effective in reducing development of cancer-related fatigue after chemotherapy. Results are more inconsistent considering aspects of physical activity. **Conclusion:** Despite inconsistent results regarding aspects of physical activity, it is fair, based on the superiority of the articles, to assume that physical activity has a good effect on fatigue in breast-, lung- and colorectal cancer patients receiving chemotherapy. That is especially compared to no physical activity as a part of the treatment. More research is still needed to provide convincing evidence on which aspects of physical activity are more beneficial. **Keywords:** Cancer, chemotherapy, fatigue, physical activity, exercise.

Sammendrag

Formål: Fatigue (tretthet), er en vanlig effekt både under og etter kreftbehandling, og det er ikke utviklet en gullstandard for å redusere fatigue. Denne litteraturstudien vil undersøke effekten av fysisk aktivitet på fatigue etter cellegift i de fire vanligste krefttypene (bryst, prostata, lunge og kolorektal), og om det er noen aspekter av fysisk aktivitet som er mer gunstig. **Metode:** PubMed, Google Scholar og ScienceDirect var databasene som ble brukt i litteratursøket for å finne relevante artikler for denne litteraturstudien. **Resultat:** Totalt ni studier ble inkludert. Hovedfunnene i litteraturstudien indikerer at fysisk aktivitet ser ut til å være effektivt på reduksjon av utvikling av kreftrelatert fatigue etter cellegift. Resultatene er mer uklare når det gjelder aspekter av fysisk aktivitet. **Konklusjon:** Det trengs mer forskning for å gi overbevisende evidens om hvilke aspekter av fysisk aktivitet som er gunstig. Til tross for uklare resultater vedrørende aspekter av fysisk aktivitet, er det grunn til å anta at fysisk aktivitet har en positiv effekt på fatigue hos pasienter med bryst-, lunge- og kolorektal kreft. Det gjelder spesielt sammenlignet med behandling uten fysisk aktivitet. **Nøkkelord:** Cellegift, fatigue (tretthet), fysisk aktivitet, kreft, trening.

Introduction

Approximately 19 million new cases of cancer emerged in 2020, and nearly half are estimated to survive the diagnosis (*Cancer Today*, n.d.). Cancer can develop virtually in the whole body, but this review will concentrate on the four types of cancer with the highest incidence in the world, which is breast, lung, prostate and colorectal (colon and rectal) cancer (*Cancer*, n.d.). These types of cancer represented an estimate of 7,8 million cases in the world in 2020, which is roughly 40% of all cases (*Cancer Today*, n.d.). They were also the most common cancer types in Norway in 2019 (Cancer Registry of Norway, 2019).

The majority of the patients with these four cancer types receive chemotherapy as a part of the treatment. Chemotherapy is a chemical drug with the aim of inhibiting cell division and eradicating tumours. It is mostly given intravenously, often in combinations of two or several drugs (Nygren, 2001). Many patients survive the diagnosis and treatment, and the National Coalition for Cancer Survivorship recommendation defines cancer survivors as "from the time of diagnosis until the end of life". Although many patients survive, chemotherapy often leads to several late effects (Wolin et al., 2012).

One of the most common late effects after chemotherapy is fatigue (Brown et al., 2011). According to Medical Subject Headings, fatigue can be defined as the occurrence of tiredness resulting from a period of mental or physical exertion (Stasi et al., 2003). Fatigue that occurs in connection with cancer diagnosis and treatment is different from fatigue experienced by the general population. Cancer-related fatigue is more severe and persistent and cannot be relieved by rest (Bower, 2014). Reinertsen el at. defines cancer-related fatigue as "a subjective feeling of tiredness, weakness or lack of energy or as an exhausting, persistent subjective sense of physical, emotional and/or cognitive tiredness that is disproportionate to the level of activity" (Reinertsen et al., 2017).

Cancer-related fatigue is known to affect quality of life after recovery and could persist for years after treatment. Fatigue also occurs during treatment, as a side effect, and could therefore be both short term side effects and late effects lasting for years. Based on the type of treatment, patient population and measurement method, the prevalence of cancer-related fatigue is estimated to range between 25% and 99%. It usually increases during treatment and decreases in the year after treatment, and the levels of fatigue before, during and after treatment vary considerably. 25-30% of cancer survivors still experience fatigue for up to 10 years after treatment (Bower, 2014). While cancer-related fatigue habitually occurs from the diagnosis itself, surgery, and other treatments, specifically chemotherapy has shown an incidence of 80% to 96% on cancer-related fatigue (Stasi et al., 2003).

There is no gold standard for the treatment of cancer-related fatigue (Bower, 2014), and it is important to identify factors that can contribute to reduced fatigue after chemotherapy. Physical activity has been substantially documented to have positive health effects in the general population. It can improve physical function (endurance, strength, flexibility), maintain a healthy body composition (Wolin et al., 2012), prevent low energy levels, and combat fatigue (Puetz, 2006). Therefore, physical activity may have the potential to reduce treatment related fatigue in cancer patients. American college of sport medicine (ACSM) points out a need for more research to provide safe guidelines on interventions focusing on exercise for cancer patients (Wolin et al., 2012). Based on this, the aim of this literature review is to examine if *physical activity can affect cancer-related fatigue in patients with common cancers (breast, colorectal, prostate, lung) receiving chemotherapy, and are there specific aspects of physical activity that are more beneficial?*

Method

Databases in this literature review included PubMed, ScienceDirect and Google Scholar. These following keywords were used in different searches: “cancer”, “cancer-related fatigue”, “fatigue”, “chemotherapy” and “physical activity”. They were connected with the term “AND” to provide relevant articles for the study. Also “Randomised controlled trial” (RCT) was selected as an option. Other keywords used to specify the searches were “lung”, “prostate”, “breast”, “colon” and “colorectal”. No standard has been used for measuring cancer-related fatigue in the various studies included in the thesis.

To be included in this study the articles had to meet the following inclusion- and exclusion criteria; Inclusion: 1) study design is RCT 2) the article is peer-reviewed and written in English or Scandinavian 3) cancer-related fatigue is reported as outcome 4) the participants received chemotherapy as a part of the treatment 5) the study included patients with at least one of the four common types of cancer (breast, colorectal, prostate and lung). Exclusion: 1) studies including other cancer types in addition to the four cancers 2) cancer-related fatigue was not obtained from measures specified for fatigue (e.g., fatigue questionnaire, fatigue scale). Two articles did not fulfil inclusion criteria number 4. Regardless, they will be included because the majority of the patients received chemotherapy, and the number of

RCTs on lung- and colorectal cancer were limited. There were in total seven articles that fulfilled all the inclusion- and exclusion criteria, and a total of nine articles were included in the review.

Results

Nine studies were included in this literature review, and had a total of 1066 patients with either lung-, colorectal- or breast cancer. No articles were found on prostate cancer patients that were RCTs and included patients who received chemotherapy as treatment. Prostate cancer is therefore excluded from the remainder of this review. Most of the studies examined the effect of aerobic training, focusing on either volume or intensity, or in combination with resistance or interval training. Two studies investigated the effect of Chinese-style exercises such as Tai Chi and Baduanjin Qigong. All patients received chemotherapy as a part of the treatment, except from Brown et al. (2018) where 87,5% of the patients were treated with chemotherapy, and an estimate of 70% of the patients in Dhillon et al (2017). The patients were randomized into either an intervention group or a control group. The main findings indicate an effect of physical activity on reducing cancer-related fatigue, but the results for different aspects of physical activity are inconsistent. Table 1 provides an overview of the characteristics in the included studies and table 2 details the intervention and results. Afterwards, each study will be described individually.

Table 1: Characteristics of the included articles.

Article (year)	Age (mean)	Cancer type	Number of participants in groups	Measure method of CRF
Dhillon et al. (2017)	64	Lung	EX=56 CG=55	Functional Assessment of Cancer Therapy-Fatigue
Zhang et al. (2016)	62,8	Lung	EX=48 CG=48	Multidimensional Fatigue Symptom Inventory
Brown et al. (2018)	nn	Colon	EX1=12 EX2=14 CG=13	Fatigue Symptom Inventory
Van Vulpen et al. (2016)	58,1	Colon	EX=17 CG=16	Multidimensional Fatigue Inventory + Fatigue Quality List
Lu et al. (2019)	55	Colorectal	EX=45 CG=45	Brief Fatigue Inventory
Van Waart et al. (2015)	51	Breast	EX1=77 EX2=76 CG=77	Multidimensional Fatigue Inventory + Fatigue Quality List
Mijwel et al. (2018)	53	Breast	EX1=79 EX2=80 CG=81	Piper Fatigue Scale
Huang et al. (2019)	48,3	Breast	EX=81 CG=78	Brief Fatigue Inventory
Husebø et al. (2014)	52,2	Breast	EX=33 CG=34	Schwartz Cancer Fatigue Scale

Abbreviations: EX = experimental intervention, CG = control group, nn= no number, CRF= cancer-related fatigue

Table 2: Intervention and results from the included articles.

Article	Intervention	Results on CRF within groups	Results on CRF between groups
Dhillon et al. (2017)	EX: 1h 45min aerobic training (S) per week + couraged to home-based training CG: usual care	EX: 38.4 to 37.5 CG: 36.3 to 36.4 P=0.62	1.2; 95% CI, -3.5 to 5.8 P=6.02
Zhang et al. (2016)	EX: 1h Tai Chi exercise (S) CG: 1h low-impact exercise Every other day during exercise time in the cycle of chemotherapy for both groups	EX: 46.0 ± 11.6 to 53.3 ± 11.8 CG: 46.8 ± 12.2 to 59.3 ± 12.2 P<0.05	EX vs. CG: 53.3 ± 11.8 vs. 59.3 ± 12.2 P<0.05
Brown et al. (2018)	EX1: 300 min*wk^{-1} of aerobic training per week (HB) EX2: 150 min*wk^{-1} of aerobic training per week (HB) CG: usual care	EX1: -5.9 ± 2.6 EX2: 0.9 ± 2.4 CG: 0.1 ± 2.5 P=0.045	EX1 vs. CG: 6.0 ± 3.6, ES: -0.75 P=0.096 EX2 vs. CG: 0.8 ± 3.5, ES: 0.08 P=0.817
Van Vulpen et al. (2016)	EX: aerobic- and resistance training 2x/week (S) moderate-vigorous intensity + 30 min PA 3x/week CG: usual care + regular PA pattern	EX: 0.0; 95% CI, -1.7 to 1.8 CG: 2.5; 95% CI, 0.7 to 4.3	-2.3; 95% CI, -4.8 to 0.2, ES: -0.7 After 36w -2.7; 95% CI, -5.2 to -0.1, ES: -0.8
Lu et al. (2019)	EX: Baduanjin Qigong 20-40 min/session 5-7 days/week (S+HB). CG: usual care	From baseline to end of intervention EX: 4.4 ± 2.2 to 2.7 ± 2.1 CG: 4.7±2.5 to 4.1±1.9 P<0.01	Moderate-severe CRF: EX: 23.2% CG: 59.1% P<0.01

Abbreviations: CRF =cancer-related fatigue, ES = effect size, HB = home-based, S=supervised, PA = physical activity, EX = experimental intervention, CG = control group, P= p-value, CI= confidence interval

Table 2 continuation

Article	Intervention	Results on CRF within groups	Results on CRF between groups
Van Waart et al. (2015)	EX1: Onco-move (HB) low-intensive PA + 30 min PA 5 days/week EX2: OnTrack (S) moderate-high resistance- and aerobic training 50 min/session, 2 sessions/week + encouraged to 30 min PA 5 days/week CG: usual care	After completed chemotherapy EX1: +3.1 EX2: + 1.7 CG: + 3.0 Follow-up period EX2: -0.6 from baseline level EX1 and CG: back to baseline levels	After completed chemotherapy EX2 vs. CG: -1.3; 95% CI, -2.6 to 0.0 ES: 0.29 EX2 vs. EX1: - 0.6; 95% CI -1.7 to 0.6 ES: 0.15 EX1 vs. CG: - 0.7; 95% CI, -1.8 to 0.5 ES: 0.21. Follow-up period: EX2 vs. CG: -1.2, ES: 0.28 EX2 vs. EX1: - 0.5, ES: 0.14 EX1 vs. CG: - 0.6 ES: 0.16
Mijwel et al. (2018)	EX1: resistance training + HIIT (S) EX2: aerobic training + HIIT (S) CG: usual care	EX1: +0.07 EX2: +1,06 CG: +1.64	EX1 vs. EX2: -0.46: 95% CI, -1.43 to 0.52 EX2 vs. CG: -0.72: 95% CI, -1.73 to 0.30 ES: -0.26 EX1 vs. CG: -1.17: 95% CI, -2.18 to -0.16 ES: -0.51
Huang et al. (2019)	EX: brisk walking (HB) 30-70% (HRR) intensity. 3-5 sessions/week 15-25 to 35-40 min CG: attentional care	EX: 0.8 to 1.4 CG: 1.0 to 1.8	EX vs. CG: coefficient -0.276 P=0.006
Husebø et al. (2014)	EX: strength training 3x/week + 30 min brisk walking/day at moderate-vigorous intensity (HB) CG: regular levels of PA	Baseline to end of chemotherapy treatment EX: 10.3±3.9 to 12.0±4.4 CG: 11.4±3.6 to 13.1±4.5 P=0.003 Baseline to 6 months EX: 10.3±3.9 to 10.4±3.3 CG: 11.4±3.6 to 10.4±3.2 P=0.181	Difference at end of chemotherapy treatment EX: +1.7 vs CG: +1.7 P=0.003 Difference from baseline to 6 months follow up EX: +0.1 vs CG: -1.0 P=0.181

Abbreviations: CRF =cancer-related fatigue, ES = effect size, HB = home-based, S=supervised, PA = physical activity, EX = experimental intervention, CG = control group, HRR= heart rate ratio, HIIT= high intensity interval training

Lung cancer

Two studies looked into the relation between physical activity and cancer-related fatigue in patients with lung cancer. A total of 208 patients were included. **Dhillon et al.** (2017) examined if "move your body" activity with a supervisor can improve cancer-related fatigue compared to usual care. Exercise was mainly aerobic, individualized to baseline. In addition, the patients were encouraged to do home-based training. No statistically significant differences were found within or between groups after intervention. Among the patients from the sample who reported increased levels of home-based physical activity during the intervention period, fatigue decreased. In those who had unchanged/reduced activity levels, cancer-related fatigue increased. The difference was reported at -4.7; 95% CI: −8.5 to −0.9; P = 0.015. **Zhang et al.** (2016) examined supervised Tai Chi exercise. This included easy movements, stretching and balance. The controls did low impact physical activity involving stretches and arm, neck and leg circles. Physical activity was performed one hour every other day from the 10th to 21st day of the chemotherapy cycle, when recovering from the response of the treatment. The study found increased levels of cancer-related fatigue within both groups, and effective responses are shown from Tai Chi with lower levels of cancer-related fatigue in the intervention group compared to the low-impact group. These results were statistically significant.

Colorectal cancer

Three studies were conducted to examine the relation between physical activity and cancer-related fatigue in colorectal cancer patients, all investigating different aspects of physical activity. A total of 162 patients were included.

Brown et al. (2018) examined the dose-response effect of physical activity on health-related quality of life including cancer-related fatigue, by comparing usual care, high-dose and low-dose aerobic exercise. The intervention was home-based and performed on treadmills. The intensity was 50%-70% of their age-estimated maximum heart rate. The low-dose group performed (EX1) 141 minutes of exercise on average per week, while the high-dose group (EX2) achieved on average 247 minutes per week. Results found decreased levels of cancer-related fatigue in the high-dose group, contrastingly increased levels were documented in the low-dose- and control group. The increased levels were highest in the low-dose group. These findings were statistically significant.

Van Vulpen et al. (2016) examined the effect of a supervised workout program combining aerobic- and resistance training compared with controls maintaining usual physical activity level. The aerobic intensity was based on HR (heart rate) and their ventilatory threshold. The strength training was carried out from percentage of 1RM. In addition, they were going to be physically active at least 30 minutes 3 other days each week. Minimum 210 minutes of moderate-vigorous activity was reported by 88% of the intervention group, and 56% of the controls. Levels of cancer-related fatigue increased with statistical significance in the controls and tended to remain unchanged in the intervention group during exercise period. The group differences tended to be lower in the intervention group after exercise period and was statistically significantly lower after 36 weeks follow-up.

The effect of Baduanjin Qigong on cancer-related fatigue, compared to a control group receiving usual care, was examined by **Lu et al.** (2019). The maximum HR was beneath 54% during the workouts, calculated as low-intensity, in the exercise group. Statistically significant decreased levels of fatigue were found in this study within both groups after intervention period. The decline was greatest in the exercise group. Halfway through the intervention period, there were no differences between the groups. The proportion of patients who experienced moderate-severe levels of cancer-related fatigue was much smaller in the exercise group versus the controls after the intervention period, with a statistically significant difference.

Breast cancer

Four studies examining the relationship between exercise interventions and cancer-related fatigue in breast cancer patients were found. A total of 696 patients were included. Two of the studies compared groups performing different intensities and combinations of exercise. **Van Waart et al.** (2015) compared low intensity physical activity and moderate- to high-intensity physical activity with a group of usual care. The low-intensity group, Onco-Move (EX1), performed a home-based, individualized programme. Subjects were also encouraged to be physically active 30 minutes 5 days per week, with an intensity equal to 12-14 on Borg scale. The second group, OnTrack (EX2), performed supervised moderate-high intensity resistance- and aerobic exercise, equal to 12-16 on Borg scale. In addition, 30 minutes activity per day was encouraged. After completing chemotherapy, increased levels of cancer-related fatigue were seen in all groups, but the increase was smallest in OnTrack. Results were similar in Onco-Move and the controls. In the six months follow up period, levels of cancer-related fatigue in the OnTrack group were lower than baseline levels, and returned to baseline levels in Onco-Move and controls. Differences between groups were greatest between OnTrack and controls, and these results were statistically significant. **Mijwel et al.** (2018) looked at the effect on conventional training modalities combined with high intensity interval training (HIIT). They used two exercising intervention groups, both doing HIIT combined with either resistance- (EX1) or aerobic training (EX2), and one control group receiving usual care. The study found that cancer-related fatigue increased in all three groups from baseline to the end of the intervention, but the increase was greatest in the patients receiving usual care, and smallest in the EX1. The increased level was statistically significantly different between EX1 and controls.

Two studies investigated the effect of home-based exercise on cancer-related fatigue in breast cancer patients. **Huang et al.** (2019) looked at the effect of Brisk walking, using one exercising group and one attentional control group. Duration, intensity, and frequency increased during the intervention period for the exercisers. The controls reported duration and mode on physical activity they spontaneously performed. This study found increased levels of cancer-related fatigue for the whole sample during intervention, but the exercisers had lower levels relative to the controls after completed intervention, and these results were statistically significant. **Husebø et al**. (2014) looked at the effect of a scheduled home-based exercise combining aerobic- and strength training. The participants were encouraged to complete 210 minutes/week of Brisk walking with moderate-vigorous intensity, plus three sessions of full body strength training. The controls were instructed to maintain their usual activity level. Mean exercise volume was 194 minutes/week in the intervention group, and 144 minutes/week in the controls. The general recommendations of 150 minutes/week were met by 58% in the intervention group and 39% in the controls. Cancer-related fatigue increased in both groups during treatment, however with no statistically significant difference between groups. The levels of fatigue were generally low in the whole sample from baseline to 6 months follow up.

Discussion

This literature review examines the effects physical activity have on cancer-related fatigue in patients receiving chemotherapy as treatment of breast-, lung- and colorectal cancer, and which aspects of exercise that are more beneficial to reduce levels of cancer-related fatigue. This review aimed to include prostate cancer, but no articles fulfilling the inclusion criteria was identified. A superiority of the included studies agree that physical activity is effective in reducing development of fatigue as they found an effect compared to the controls, except from Dhillon et. al (2017) and Husebø et al. (2014). Nevertheless, Dhillon et al. (2017) found good effects in the patients who increased home-based exercise among the entire sample, and the whole sample in Husebø et al. (2014) had generally low fatigue levels throughout the intervention and follow up period. Therefore, this review found that physical activity appears to be effective in reducing the development of cancer-related fatigue during chemotherapy and can reduce cancer-related fatigue post-treatment. Results are more inconsistent regarding aspects of physical activity, but favours moderate-high intensity, the combination of resistance- and aerobic-, Chinese-style- and high-volume exercise as the most promising aspects to combat cancer-related fatigue.

Intensity

Good effects are seen at high intensity physical activity. That applies to both resistance- and aerobic exercise. Former research has yet to find out which intensity is more effective on cancer-related fatigue (Reinertsen et al., 2017), although Van Vulpen et al. (2016), Van Waart et al. (2015) and Mijwel et al. (2018) comparably found high intensity physical activity effective on cancer-related fatigue. Low to moderate intensity does not seem to give any consistency in this review, and the results indicate that other aspects such as type of physical activity, duration and volume play a bigger role at lower intensity. Although, ACSM recommends 150 minutes of moderate intensity or 75 minutes of high intensity physical activity to gain important health benefits for cancer patients (Wolin et al., 2012), which implies that moderate to high intensity could be effective on cancer-related fatigue.

Physical activity at low-moderate intensity (e.g., walking) does not require testing before participation. Patients who want to perform high intensity physical activity should undergo clinical testing by professionals to perform exercise safely. High intensity and physical activity in general could be feasible and safe when precautions and individual testing are performed. However, cancer patients are a heterogenous group and the feasibility could be limited for some patients. Although physical activity is feasible, there are some contraindications for cancer patients, such as comorbid factors and extreme anaemia. Exercise should be consulted with professionals and performed with caution (Wolin et al., 2012).

Volume

It is important to consider that this sample is a heterogeneous group. Therefore, factors such as exercise volume can play an important role in achieving a good effect on cancer-related fatigue. As mentioned, not everyone is able to perform high-intensity training, so a large volume could be important. A high volume with moderate intensity seems effective to reduce cancer-related fatigue according to the results of Brown et al. (2018). Due to the outcomes, there is reason to believe that the volume of physical activity should be higher than 150 minutes of moderate activity per week to reduce cancer-related fatigue. This finding is also seen in Husebø et al. (2014) where the levels of fatigue was generally low in the entire sample from baseline to 6 months follow-up, and the intervention group had a higher exercise volume than 150 minutes per week, and the control group almost reached the same volume. Dhillon et al. may indicate that low frequency and a short exercise period is not sufficient to obtain an effect on cancer-related fatigue. But of those who increased home-based training in the entire sample the levels of cancer-related fatigue were reduced. This indicates that a higher volume can help reduce cancer-related fatigue. This is supported by findings in former studies (Puetz, 2006).

Type of training

Aerobic training, combination of resistance- and aerobic training, and Chinese style exercise is the type of training used in the included studies, and they have shown good effects on cancer-related fatigue. This is similar to research where it is suggested that these types of exercise are effective in helping cancer patients through the course of the disease, the treatment and the time after, and thus contribute to an increased quality of life including cancer-related fatigue (Mustian et al., 2012). Three studies examined the effect of aerobic training alone. Brown et al. (2018) and Huang et al. (2019) found good effects on cancer-related fatigue in their intervention group, and Dhillon et al. (2017) did not, suspiciously due to the low exercise volume. Aerobic exercise demonstrates effective interventions for cancer patients and cancer survivors on cancer-related fatigue and quality of life, as well on anxiety, depression, sleep disorder and cardiopulmonary function (Mustian et al., 2012).

Four of the studies used a combination of aerobic- and resistance training in the intervention, and three of them showed good effects on cancer-related fatigue. Van Vulpen et al. (2016) Van Waart et al. (2015) and Mijwel et al. (2018) show similar effects that involve no change or little reduction or small increase in fatigue from baseline values. However, Husebø et al. (2014) did not find any significant effect, and it is a reason to believe that the poor adherence to the intervention played an important role in the outcome and can limit the interpretation of the results somewhat. Meta-analyses have previously shown that combining resistance training and high-intensity aerobic training have a greater effect on cancer-related fatigue than aerobic training alone (Meneses-Echávez et al., 2015). Furthermore, it improves quality of life, muscle strength and function, cardiorespiratory capacity, and immune function (Mustian et al., 2012). None of the studies examined only resistance training, but previous research shows good effects both during and after cancer treatment as it reduces side effects, provides better quality of life and strengthens the tolerance for high doses of chemotherapy in patients (Mustian et al., 2012). ACSM guidelines for physical activity for the general population encourage and recommend performing a combination of resistance and aerobic exercise to achieve a range of positive outcomes (Wolin et al., 2012). Therefore, it could also play a role in reducing and preventing further increase of cancer-related fatigue, as seen in several of the articles. All the studies with combination aerobic and resistance have used high intensity, and this combination seems effective.

Baduanjin Qigong and Tai Chi are mindfulness-based exercises and have been shown to be effective in two of the studies (Huang et al., 2019 & Lu. Et al., 2019) on lung and colorectal cancer on reducing the development of and the strength of perceived fatigue. In cancer patients, these forms of exercise have shown significant benefits. A 12-week Tai Chi Chuan program for breast cancer patients found improved quality of life and side effects. Consequently, these attention-based exercises can be effective in patients if they practice this with moderate intensity and a proper volume (Mustian et al., 2012).

Home-based vs supervised training program

Supervised exercise has been shown more effective in comparison to home-based exercise in the included RCTs, and supervised patients had better adherence to the intervention program. This could indicate that supervised exercise gives more motivation to complete an exercise program. Earlier reviews confirm that supervised workouts are effective (Meneses-Echávez, 2015). Although, home-based exercise has shown effects on reducing fatigue and is a viable alternative for patients not able or willing to participate in supervised exercise (Van Waart et al., 2015).

Methodological aspects, validity, and reliability

Zhang et al. (2016), Brown et al. (2018) & Van Vulpen et al. (2016) conclude that the selection of patients should have been larger for a more reliable result. Weaknesses with low study population may be due to low precision and increased risk of selection bias. It could be difficult to assess an effect of the intervention because there is a greater chance of an influence of coincidences in the outcomes, and it limits the validity of conclusions because of low statistical power. Length of the intervention can also affect the results. Dhillon et al. extends over a short amount of time, as well as it does not show any good results. The length of these studies varies from 8-24 weeks, and this variation in time may be one of the reasons for the different results. In addition, it may be possible that relevant articles may have been excluded by mistake. If this had been avoided, the results may have looked different.

Scientists have developed several methods for measurement, based on experienced fatigue, sleep, lack of energy, subjective stress, depression, and the effect of cancer-related fatigue in daily activities. It is difficult to get valid and reliable results when measuring fatigue, hence there is no gold standard (RN et al., 2007). The articles in this review could be influenced by this because they used different methods to measure fatigue, both subjective and objective. Several of these measures require self-assessments, where patients can struggle to define experienced fatigue. This may be a factor restricting the validity and generalization of the findings. Further, it will be important to prepare more comprehensive and general measures for fatigue (RN et al., 2007).

All patients received chemotherapy as a part of the treatment, except from Brown et al. (2018) where 87,5% were treated with chemotherapy, and an estimate of 70% in Dhillon et al. (2017). This challenges the interpretation of physical activity on cancer-related fatigue from chemotherapy. Moreover, the selection of RCTs on some cancer types receiving chemotherapy were somewhat limited, resulting in few studies on lung- and colorectal cancer.

This literature review is strengthened by the use of only RCTs. RCT is considered the gold standard and most adequate study design to avoid selection bias and confounders, and provides an isolated effect of the intervention (Munnangi & Boktor, 2021). In addition, all primary articles included are peer reviewed to ensure quality control.

Knowledge needs

The findings in this review strengthen the presumptions from previous research that physical activity is effective in reducing and combating cancer-related fatigue on all the included cancer types. However, it does not provide sufficient and unambiguous evidence to conclude firmly. The population should be larger to get clearer and more noticeable results, which is supported by findings in Mustian et al. (2012). There are not enough articles studying the separate cancer types, and interventions are not comparable regarding aspects, because the exercise type, intensity and volume varies. In further studies the variation of interventions should be smaller. (E.g., compare different intensities or types of physical activity only).

Conclusion

Based on the findings in this review it is safe to conclude that physical activity has a favourable effect on cancer-related fatigue after chemotherapy treatment in the most common cancer types, especially compared to usual care. Moderate-high intensity, the combination of resistance- and aerobic-, Chinese style- and high-volume exercise all have indicated good results. There are insufficient grounds to identify or recommend one aspect that gives the greatest possible effect on cancer related fatigue. This is due to the restricted sample of primary articles in the review and their methodological limitations, as well as the difficulty of comparing the aspects because of the variations seen between the interventions. In addition, it must be taken into account that cancer populations are very heterogeneous, and exercise should be tailored individually. With this in consideration, further research should address larger study populations, as well as comparing different aspects and types of exercise.

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