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Effect of physical exercise intervention on daily sleep quality in women with breast cancer and severe depressive or anxiety symptoms: a series of N-of-1 trials

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Conflict of Interest: The authors declare that they have no conflict of interest.

Data availability: Data are available <https://osf.io/h95ae/>

Ethic approval statement: The research protocol has been approved by the Ethics Boards of the Eastern Montreal Integrated University Health and Social Services Centre (2022-4319).

Clinical registration: The study protocol was registered a priori (doi:10.17605/OSF.IO/9SBJH).

Abstract

Aim

The aim of this preliminary study was to examine the effects of a 12-week remote supervised physical activity intervention on daily self-reported sleep quality among women with breast cancer and severe depressive and anxiety symptoms.

Method

A series of N-of-1 trials with an A-B-A' design was carried out with ecological momentary assessments. Phase A and A' (2-week) represented pre- and post-intervention measures and phase B represented the intervention phase. Participants received a daily prompt to report their sleep quality. Sixteen participants completed the treatment.

Results

Sixteen out of eighteen participants completed the intervention. Participants' age ranged from 29 to 61 years old, and 10 were included during their cancer treatment. A significant improvement of sleep quality was observed in 9 participants with moderate to large effects. However, the intervention had a moderate and significant negative effect on the sleep quality in 2 patients.

Conclusion

This is the first study to show that physical activity is potentially effective in women with breast cancer and severe depressive and anxiety symptoms. The findings justify extension to a randomized controlled trial.

Keywords

Telehealth, cancer, insomnia, physical exercise, single case experimental study

Funding: This research received a grant of Fondation Cancer du Sein du Québec.

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Introduction

Poor sleep quality is highly prevalent in breast cancer patients, particularly in women with severe depressive or anxiety symptoms (1). Regarding treatment options, physical activity and cognitive behavioral therapy have a similar effectiveness (2) for breast cancer. Additionally, previous reviews suggested that physical activity interventions are associated with a better sleep quality in cancer patients with or without sleep difficulties (3). However, to date, the effects of physical activity on sleep quality has not been explored among women with breast cancer and severe depressive and anxiety symptoms. The potential benefits of physical exercise on sleep outcomes could vary widely between participants (4). A previous investigation found a physical activity intervention response heterogeneity on sleep outcomes in breast cancer women (5). Those authors recommended examining physical activity intervention benefits on sleep parameters at the intra-individual level (4).

Thus, this preliminary study aims to investigate the effects of a 12-week remote supervised physical activity intervention on daily self-reported sleep quality at the individual level among breast cancer patients with severe depressive and anxiety symptoms.

Method

The study protocol was registered a priori (<https://osf.io/9sbjh>) and has been approved by the Ethics Boards of the Eastern Montreal Integrated University Health and Social Services Centre (2022-4319) (6). We carried out a series of N-of-1 with an A-B-A' design combined with ecological momentary assessments in collaboration with the psycho-oncology services of two hospitals (Montreal, Canada). Each A phase (2 weeks each) represented the pre- and post-intervention baseline measures, and the B phase (12-week) represented the intervention phase. In this multi-phase experimental design, participants served as their own control. This method is particularly suitable to assess the effect of interventions among people with comorbidity and more difficult to reach for behavioral interventions (7). We recruited inactive women with breast cancer and a severe level of self-reported depressive

(Patient Health Questionnaire [PHQ-9] score ≥ 15) or anxiety symptoms (General Anxiety Disorder [GAD-7] questionnaire score ≥ 15) (8). PHQ-9 and GAD-7 are both recommended questionnaires by the Canadian Association of Psychosocial Oncology (8).

For the entire 16 weeks, participants received a daily prompt in their phone to report their sleep quality. Sleep quality measure was the following item “During last night, my sleep quality” was adapted from the Consensus Sleep Diary (9). A 0-100 visual analog scale (0: very bad - 100: excellent) has been preferred because it has been associated with better psychometric characteristics than Likert scales at within-person level (10), it is more appropriate with daily measures and well-accepted by adults with mental health disorders (11).

Three repeated measures of insomnia symptoms were also measured to increase the external validity of the study. The Insomnia Severity Index (ISI) was filled by participants pre- and post- first phase A and end of phase B. ISI has been recommended by the Canadian Association of Psychosocial Oncology to assess sleep disorders among adults with cancer (12).

Our 12-week personalized intervention included 2 to 3 weekly supervised remote physical activity sessions (aerobic training + yoga or resistance training). The length of sessions was gradually extended from 30 to 60-min, to ensure a good adherence rate. Participants had 3 supervised physical activity sessions from week 1 to 4. From week 5 to 12, participants had 2 supervised remote physical activity sessions, with the choice between supervised or unsupervised sessions for the third weekly session. Also, participants could decide for the second part of each supervised session, to perform resistance or yoga exercise after mandatory aerobic exercise (details are available in (13)). Our intervention was adapted for delivery via Zoom videoconferencing and required minimal technical skills. The physical activity sessions were supervised by three kinesiologists who had a 20-hour training focusing on physical activity intervention implementation and therapeutic alliance development.

Sleep quality data were analyzed with a Tau-U, a non-parametric test providing effect size estimates allowing to control observed trends in both phases (14). Two Tau-U coefficients were calculated for

each participant (i.e., phase A vs B, phase A vs A'). Our analyses were controlled for baseline trends. An effect size of less than 0.20 was interpreted as a small effect; 0.20-0.60 a moderate effect; 0.60-0.80 a large effect; and 0.80 or above a very large effect (14). Analyses and graphics were performed with R 4.4 and ggplot2, and scan packages (15). Data and R scripts are available online (<https://osf.io/h95ae/>).

Results

Eighteen participants were recruited, but two dropped out of the intervention (due to personal issues). Participants' age ranged from 29 to 61 years old, and 10 were included during their cancer treatment (chemotherapy or radiotherapy) (see descriptive table in Supplementary file). The adherence rate to physical activity sessions was 85% (min 32%, max 100%). No participants showed spontaneous or unexpected reactions (e.g., hypotension) during the supervised online training or any adverse events.

Regarding scores of ISI, 7 and 9 experienced clinical level sleep disorders (i.e., ISI score ≥ 8) and insomnia syndrome (i.e., ISI score ≥ 15), respectively. Figure 1 represents the daily sleep quality score for each phase. Figure 2 shows the individual ISI scores and Tau-U findings.

A significant improvement of sleep quality during the intervention was observed in 7/16 participants (with moderate to large effect sizes). Among them, 5 had also a significant higher sleep quality after the intervention with moderate effect sizes. Two others reported a significantly improved sleep quality only after the intervention (with moderate to large effect sizes) but not at follow-up. However, two effects were significantly negative for id1 and id9 during and after the intervention, respectively. A visual analysis of repeated ISI scores (Figure 3) showed that self-reported sleep disorder risk was still high at the end of the intervention.

Discussion

The benefits of a physical activity intervention in our study were found among 9/16 participants. This result is very encouraging and reflects the heterogeneity of the influence of physical activity on sleep. The positive effects of physical activity have been observed at different timing: only during or after the intervention and maintained during the follow-up phase. This is line with the heterogeneous responses

found in studies examining the short or mild term benefits of physical activity on sleep quality (3). One unexpected finding was the significant negative impact of our intervention for two participants. This finding is contrary to a previous meta-analysis that did not identify a detrimental effect of physical activity on sleep quality in patients with cancer and sleep disorders (16).

Two possible explanations could reflect the nonsignificant effect of our intervention. Firstly, our intervention may not have improved enough the cardiorespiratory fitness of study participants. Indeed, the aerobic fitness has been found to be a moderator of physical activity intervention on self-reported sleep quality in the context of breast cancer (17). Secondly, a ceiling effect can be observed for one participant (id5) in Figure 1. Her sleep quality level was relatively high during the phase, even though her ISI score was high. The sleep quality deterioration observed for two participants may be related to nocturnal hot flashes frequency (18) or antiestrogen endocrine therapies (19). Hot flashes are more frequent in breast cancer patients, and higher frequency is associated with higher physical activity level (18). Thus, our intervention could have increased the occurrence of nighttime hot flashes and decrease the sleep quality.

Although this study employed a robust method, our preliminary results have to be replicated. Given the small sample size, recruited in two hospitals, the generalization of the results to larger population and other contexts is limited. The current design study may be improved with a passive and continuous measure of sleep parameters (e.g., actimetry), data collection about hot flashes in daily ecological momentary assessments and a detailed characterization of possible endocrine treatments.

In conclusion, our 12-week physical activity intervention has shown promising results for improving sleep quality in women with breast cancer and severe psychological distress. This is the first study to show that physical activity is potentially effective in women with breast cancer and a psychological distress comorbidity. The findings justify extension to a randomized controlled trial. If effective, our online intervention may facilitate its dissemination to kinesiologists, exercise physiologists, and patients.

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Physical exercise and sleep quality in breast cancer context

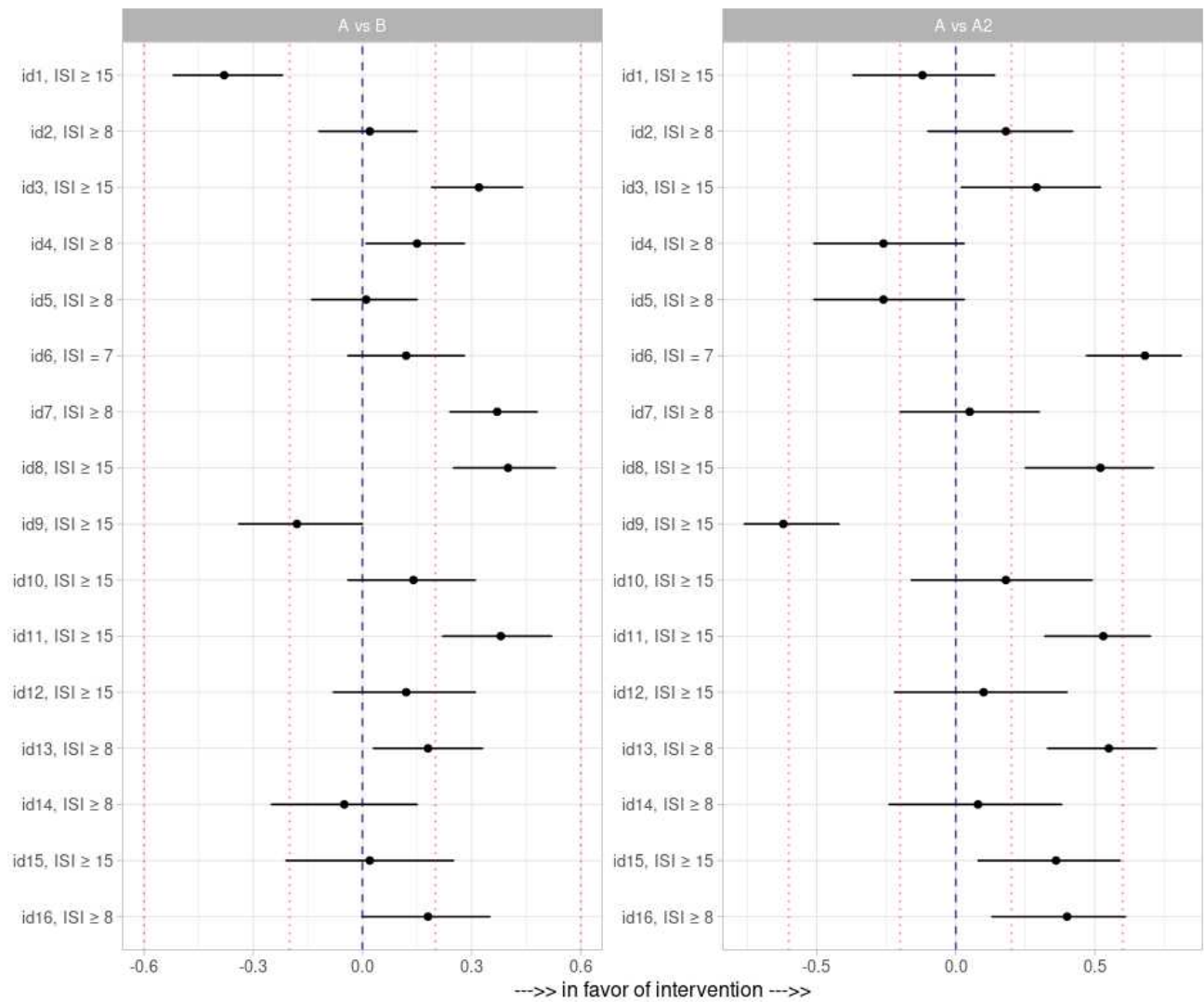
Figure 1. Daily self-reported sleep quality by phase (local regressions)



Notes. A = first observational phase; B = intervention; A2 = second observational phase

Physical exercise and sleep quality in breast cancer context

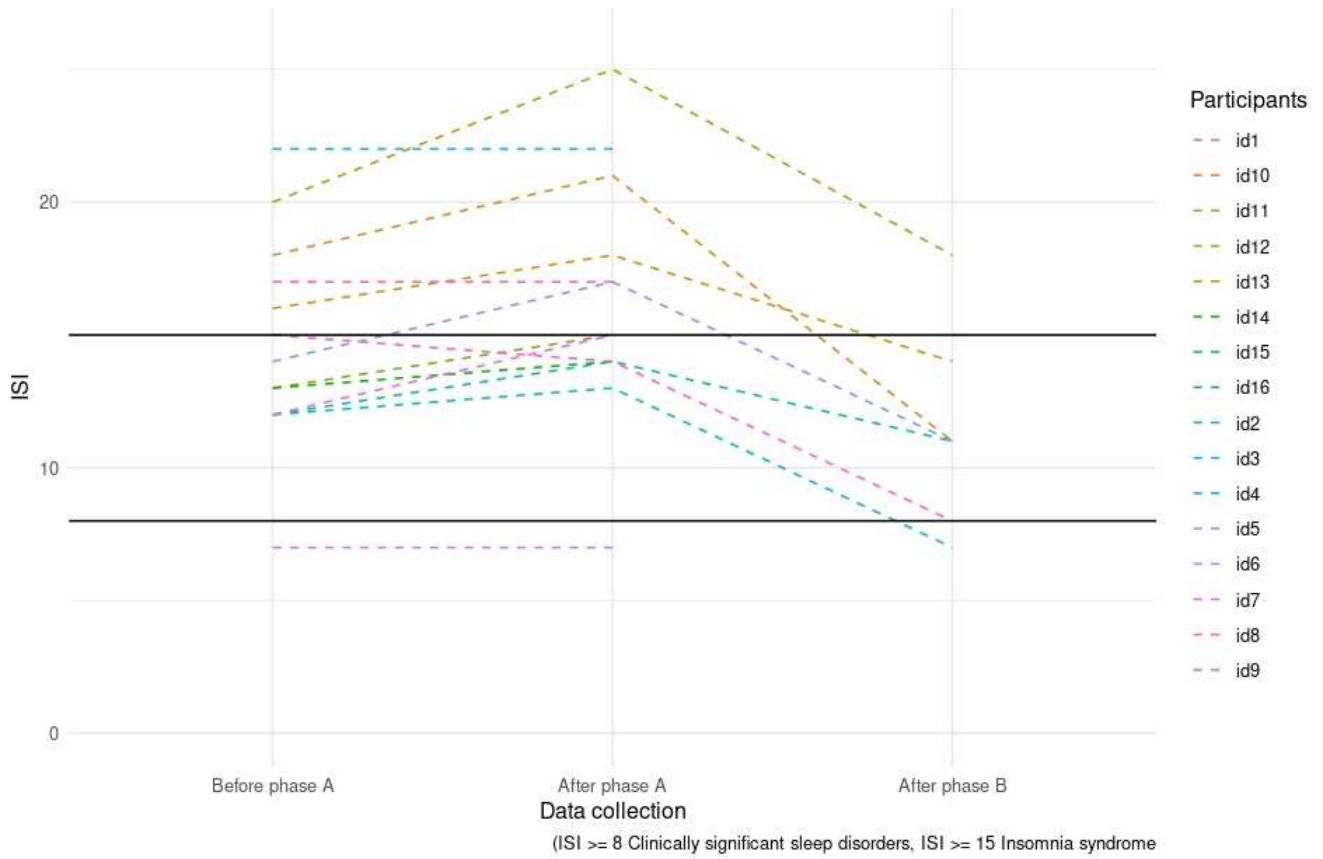
Figure 2. Forest plots showing findings from *Tau-U* statistics



Notes. Red dotted lines represent the thresholds for interpretation; A = first observational phase; B = intervention; A2 = second observational phase

Physical exercise and sleep quality in breast cancer context

Figure 3. Insomnia severity index score for study participants



Notes. ISI = Insomnia severity Index