Exercise Training on Depressive Symptoms in Cancer Patients

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Cancer patients need to overcome several issues, leaving them more vulnerable to depressive symptoms. Exercise is recognised as a practice that helps to deal with depressive symptoms. This research includes meta-analyses about the effect of exercise on depressive symptoms among cancer patients. Six studies were included. A significant reduction in depressive symptoms was observed because of exercise. However, the studies varied in methodological terms, making a broad generalisation difficult. It can be concluded that exercise is a good alternative to deal with depressive symptoms among cancer patients. Still, more studies are needed to clarify some aspects that are not answered yet.

Keywords: tumour ; exercise ; depression ; mental health ; cancer survivorship

1. Introduction

Cancer is a global public health issue, with 19.3 million new cases of cancer diagnosed in 2020 and 10 million individuals dying from the disease [1]. Cancer occurs mostly with older age and in the United States of America, and 90% of cancers are diagnosed in those aged >50 years [2]. Female breast cancer is the most commonly diagnosed cancer (11.7%), followed by lung (11.4%), colorectal (10.0%), prostate (7.3%), and stomach (5.6%) cancers [1]. Despite the lethality of different types of cancer, many cancer patients survive. However, cancer patients are in a vulnerable situation since they go through several health challenges, as cancer diagnosis and treatment have a serious impact on their physical and mental well-being [3]. Cancer patients experience several emotional disruptions, such as fear of death, interruption of life plans, decreased body image and self-esteem, and changes in social role and lifestyle [4]. One of the most common impacts is depression, which affects up to 20% of patients with cancer [5], however, the prevalence rate of depression among cancer patients is heterogeneous, according to clinical setting [6], the stage of the disease [5][7] and type of cancer [8], ranging between 5% and 49% [9]. Aggravating this issue, depression in cancer patients is associated with low chemotherapy compliance [10] and an increased risk of death [11]. Therefore, the treatment of depression among cancer patients should be a priority. However, there is still the notion that depression is inevitable and untreatable [12]. In addition, there is limited trial data on depressive symptoms' treatment efficacy in cancer patients [13]. Pharmacological therapy, consisting of antidepressant medications, is usually considered for the treatment of moderate to severe major depression; also, a combined modality approach, including psychosocial and pharmacologic interventions, is a feasible alternative [14].

Alongside pharmacological and psychosocial therapy, exercise can have a positive impact on depressive symptoms [15]. Several mechanisms are involved in the association between exercise and depression, from neurobiological to behavioural mechanisms [16]. One is the inflammation-related factors (IRFs) [17], where studies have shown an association between inflammatory markers and depressive symptoms, including fatigue, impaired sleep and cognitive dysfunction [18] [19]. Exercise could create an anti-inflammatory environment and reduce the serum level of leptin and fibroblast growth factors (FGF) [20]. IL-10, produced by exercise, acted as an anti-inflammatory cytokine and is stimulated by the release of adrenaline and cortisol from the adrenal gland, which reduces the release of pro-inflammatory cytokines in the hippocampus [21]. Regarding behavioural mechanisms, exercise can promote several behavioural changes. Engagement in exercise programs and learning new movements skills or completing physically challenging exercises may lead to gaining a sense of mastery [22]. The activity-based perception of physical strength and flexibility is associated with increased physical self-esteem and consequently, an increase in global self-esteem [23].

Regular exercise after diagnosis increases survivorship by 50–60%, with strong evidence for breast and colorectal cancers [15]. In addition to improving depressive symptoms, exercise positively impacts other depression- and cancer-related outcomes, such as anxiety, fatigue, physical functioning, and health-related quality of life [3]. Although the efficacy of exercise interventions in reducing depressive symptoms among cancer patients was already established by previous systematic reviews and meta-analyses [24][25][26][27][28][29], previous studies substantially vary in scope, quality and

methodology, which can cause considerable confusion and misdirect efforts in the implementation of exercise interventions. Meta-analyses of previous researches are warranted to better inform future trials needs, as well as establish a consistent message for health policies targeting this vulnerable population. The specific questions that the researchers should answer with this research are: (1) regarding some aspects of exercise intervention, such as the type of exercise, the dose of exercise, the difference between home-based exercise and other locations, which are the most effective to deal with depressive symptoms? (2) Regarding the difference between the type of cancer, the moment of the exercise intervention, before, during or after cancer treatment, are there any differences?

2. Current Insights

This research included six meta-analyses that comprised 100 individual studies with little overlap that investigated the effect of exercise on depressive symptoms among cancer survivors. Overall, a small significant reduction in depressive symptoms in this vulnerable population was observed in the studies. However, high-quality evidence for the efficacy of exercise on depressive symptoms is limited. For a more detailed analysis, some points need to be considered, such as the type of cancer, the specificity of exercise prescription, the time of interventions, and during or after cancer.

In this research, participants had mainly breast cancer in the included meta-analysis and were mostly women. Only one study did not include breast cancer [27] and was with prostate cancer patients, and it was the one that did not observe a significant effect of exercise on depressive symptoms. In a subgroup analysis, Brown et al. found a significant reduction in depressive symptoms among breast cancer survivors but did not find the same in prostate, leukaemia, lymphoma and colorectal cancer [17]. The prevalence of depression among breast cancer survivors is higher than in other cancers and can achieve 32.8% [30]. Moreover, depression is more prevalent in women than men [31], and breast cancer is prevalent in women. Evidence suggests that depression in breast cancer patients decreases over time and is more common throughout the disease and in the recurrent phase of breast cancer [32]. The occurrence of depression among patients with breast cancer is due to several factors, such as treatment-related distress, worries regarding fear of death and disease recurrence, and altered body image, sexuality and attractiveness [33][34][35]. In addition, a study exposes the association between depression and tumour levels of estrogen receptors and progesterone receptors [36]. A study found that fatigue and pain are significant risk factors for developing depression among breast cancer survivors [32]. Fatigue is also a recognised barrier to exercise [37]; however, exercise can reduce fatigue among women with breast cancer [38]. The benefits of exercise can be extended to improve physical functioning and multiple aspects of quality of life among cancer patients [39]. Moreover, exercise is a feasible alternative to control symptoms burden and improve well-being among breast cancer patients [34].

Another sample characteristic that must be highlighted is that most patients were older adults (>50 years old). In the general population, the prevalence of depression symptoms rises with increasing age, 10% to 15% of older adults have clinically significant depressive symptoms [40]. Older patients with cancer often experience depression, fatigue, pain, and sleep disturbance [41]. Only one included meta-analysis directly explored the role of age in the effectiveness of exercise on depression symptoms and found that the efficacy seems to disappear among old age patients [24]. However, an RCT with older cancer patients receiving chemotherapy found that after the six-week structure exercise program, participants' anxiety and mood improved [42]. Besides the effects of exercise on mental health, physically active old age patients improve general health, such as physical fitness outcomes, quality of life and increased life expectancy [43].

When considering the effects of exercise on depressive symptoms, it is necessary to consider the characteristics of the exercise the researchers are referring to. Many dimensions of exercise exist, which are captured in part by the principle (frequency, intensity, time and type of exercise), as well as the way of practising, whether accompanied or not and if exercise occurs indoors or outdoors. However, the included systematic meta-analyses showed great variance concerning exercise. Except for Gonzalez et al. and Yi et al. [26][29], which analysed the effects of yoga intervention, the others included meta-analyses that examined a variety of exercises, such as aerobic (e.g., walking, cycling), resistance (e.g., weight machine, resistance bands) and qigong. Only the Patsou et al. study explored the difference between the types of exercise and found that aerobic intervention yields a large significant effect on depressive symptoms. At the same time, resistance training presents a small significant effect, and combined aerobic and resistance training yielded a moderate effect [27]. This statement is in accordance with the American College of Sports Medicine (ACSM), which describes that resistance training alone does not seem effective for depression [3]. Aerobic activities are cost-effective and should be popularised in clinical practice.

Regarding yoga, both included meta-analyses that analysed only intervention found significant and medium effects on depressive symptoms [26][29]. However, in the Patsou et al. study, which included aerobic exercise, resistance exercise and yoga intervention, when a subgroup analysis proceeded and considered only yoga intervention, no significant

difference in depression symptoms was observed [27]. The contradictory results found in the three studies can be explained by the fact that yoga combines breathing (pranayama) and meditative techniques during a series of postures (asanas), but different types of yoga were being practised, which made it difficult to understand the effects of this practice [44].

Two included meta-analyses found that supervised exercise is more efficient than non-supervised exercise [33][45], which also appears in the ACSM recommendation [3]. Craft et al.'s study [25] explored the effects of exercise session durations and found that more than 30 min had larger effects compared with less than 30 min of the exercise session. In Patsou et al. [27] ≤135 min/week yielded a moderate to large effect and no effect with ≥135 min/week of exercise. The ACSM describes that aerobic training performed three times per week and for at least 12 weeks or twice weekly with combined aerobic plus resistance training lasting 6 to 12 weeks, can significantly reduce depressive symptoms in cancer survivors during and after treatment. However, the exact exercise duration per week has not yet been established by the ACSM. Gonzalez et al.'s study [26] explored the frequency and found no differences between one class per week and two or more classes per week. In contrast, Patsou et al. [27] explored the exercise intervention program duration and found that exercise for up to 12 weeks yielded a moderate to large effect compared with a small effect of over 12 weeks. Aside from the efficacy of depressive symptoms, exercise has other benefits in health outcomes among cancer survivors that must be considered such as improving cardiorespiratory fitness [46], and muscle strength [47][48].

Another important aspect of the efficacy of exercise on depressive symptoms among cancer survivors is the time of intervention, before the diagnosis, during treatment or in a recovering phase. This aspect was explored, and no difference was found between patients receiving cancer treatment, following treatment or mixed treatment status [26]. On the other hand, patients under treatment yielded a moderate effect, and patients post-treatment yielded a small effect [27]. Exercise increases the chemotherapy completion rate during treatment without causing lymphedema or significant adverse events [49]. In addition, exercise appears to reduce chemotherapy-induced peripheral neuropathy symptoms in patients receiving taxane-, platinum-, or vinca alkaloid-based chemotherapy [50].

References

1. Sung, H.; Ferlay, J.; Siegel, R.L.; Laversanne, M.; Soerjomataram, I.; Jemal, A. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J. Clin. 2021, 71, 209–249.
2. Siegel, R.L.; Miller, K.D.; Jemal, A. Cancer statistics, 2018. CA Cancer J. Clin. 2018, 68, 7–30.
3. Campbell, K.L.; Winters-Stone, K.M.; Wiskemann, J.; May, A.M.; Schwartz, A.L.; Courneya, K.S. Exercise guidelines for cancer survivors: Consensus statement from international multidisciplinary roundtable. Med. Sci. Sports Exerc. 2019, 51, 2375–2390.
4. Pasquini, M.; Biondi, M. Depression in cancer patients: A critical review. Clin. Pract. Epidemiol. Ment. Health 2007, 3, 2.
5. Mitchell, A.J.; Chan, M.; Bhatti, H.; Halton, M.; Grassi, L.; Johansen, C. Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: A meta-analysis of 94 interview-based studies. Lancet Oncol. 2011, 12, 160–174.
6. Naser, A.Y.; Hameed, A.N.; Mustafa, N.; Alwafi, H.; Dahmash, E.Z.; Alyami, H.S. Depression and anxiety in patients with cancer: A cross-sectional study. Front. Psychol. 2021, 12, 585534.
7. Caruso, R.; Nanni, M.G.; Riba, M.; Sabato, S.; Mitchell, A.J.; Croce, E.; Grassi, L. Depressive spectrum disorders in cancer: Prevalence, risk factors and screening for depression: A critical review. Acta Oncol. 2017, 56, 146–155.
8. Pilevarzadeh, M.; Amirshahi, M.; Afsargharehbagh, R.; Rafiemanesh, H.; Hashemi, S.-M.; Balouchi, A. Global prevalence of depression among breast cancer patients: A systematic review and meta-analysis. Breast Cancer Res. Treat. 2019, 176, 519–533.
9. Walker, J.; Holm Hansen, C.; Martin, P.; Sawhney, A.; Thekkumpurath, P.; Beale, C. Prevalence of depression in adults with cancer: A systematic review. Ann. Oncol. 2013, 24, 895–900.
10. Ayres, A.; Hoon, P.W.; Franzoni, J.B.; Matheny, K.B.; Cotanch, P.H.; Takayanagi, S. Influence of mood and adjustment to cancer on compliance with chemotherapy among breast cancer patients. J. Psychosom. Res. 1994, 38, 393–402.
11. Onitilo, A.A.; Nietert, P.J.; Egede, L.E. Effect of depression on all-cause mortality in adults with cancer and differential effects by cancer site. Gen. Hosp. Psychiatry 2006, 28, 396–402.
12. Dwight-Johnson, M.; Ell, K.; Lee, P.J. Can collaborative care address the needs of low-income Latinas with comorbid depression and cancer? Results from a randomised pilot study. Psychosomatics 2005, 46, 224–232.

13. Laoutidis, Z.G.; Mathiak, K. Antidepressants in the treatment of depression/depressive symptoms in cancer patients: A systematic review and meta-analysis. BMC Psychiatry 2013, 13, 140.

14. Rodin, G.; Katz, M.; Lloyd, N.; Green, E.; Mackay, J.A.; Wong, R.K.S. The treatment of depression in cancer patients: A systematic review. Supportive Care Cancer 2007, 15, 123–136.

15. Newton, R.U.; Galvão, D.A. Exercise in prevention and management of cancer. Curr. Treat. Options Oncol. 2008, 9, 135–146.

16. Smith, P.J.; Merwin, R.M. The role of exercise in management of mental health disorders: An integrative review. Annu. Rev. Med. 2021, 72, 45–62.

17. Yuan, N.; Chen, Y.; Xia, Y.; Dai, J.; Liu, C. Inflammation-related biomarkers in major psychiatric disorders: A cross-disorder assessment of reproducibility and specificity in 43 meta-analyses. Transl. Psychiatry 2019, 9, 233.

18. Bower, J.E.; Huedo-Medina, T.B.; Pescatello, L.S.; Ryan, S.M.; Pescatello, S.M.; Moker, E. Fatigue and proinflammatory cytokine activity in breast cancer survivors. Psychosom. Med. 2002, 64, 604–611.

19. Motivala, S.J.; Sarfatti, A.; Olmos, L.; Irwin, M.R. Inflammatory markers and sleep disturbance in major depression. Psychosom. Med. 2005, 67, 187–194.

20. Fedewa, M.V.; Hathaway, E.D.; Ward-Ritaco, C.; Williams, T.D.; Dobbs, W.C. The effect of chronic exercise training on leptin: A systematic review and meta-analysis of randomized controlled trials. Sports Med. 2018, 48, 1437–1450.

21. Moon, H.Y.; Kim, S.H.; Yang, Y.R.; Suh, P.-G. Macrophage migration inhibitory factor mediates the antidepressant actions of voluntary exercise. Proc. Natl. Acad. Sci. USA 2012, 109, 13094–13099.

22. Gheysen, F.; Poppe, L.; DeSmet, A.; Swinnen, S.; Cardon, G.; De Bourdeaudhuij, I.; Chastin, S.; Fias, W. Physical activity to improve cognition in older adults: Can physical activity programs enriched with cognitive challenges enhance the effects? A systematic review and meta-analysis. Int. J. Behav. Nutr. Phys. Act. 2018, 15, 63.

23. Ryan, M.P. The antidepressant effects of physical activity: Mediating self-esteem and self-efficacy mechanisms. Psychol. Health 2008, 23, 279–307.

24. Brown, J.C.; Huedo-Medina, T.B.; Pescatello, L.S.; Ryan, S.M.; Pescatello, S.M.; Moker, E.; LaCroix, J.M.; Ferrer, R.A.; Johnson, B.T. The efficacy of exercise in reducing depressive symptoms among cancer survivors: A meta-analysis. PLoS ONE 2012, 7, e30955.

25. Craft, L.L.; VanIterson, E.H.; Helenowski, I.B.; Rademaker, A.W.; Courneya, K.S. Exercise effects on depressive symptoms in cancer survivors: A systematic review and meta-analysis. Cancer Epidemiol. Biomark. Prev. 2012, 21, 3–19.

26. Gonzalez, M.; Pascoe, M.C.; Yang, G.; de Manincor, M.; Grant, S.; Lacey, J.; Firth, J.; Sarris, J. Yoga for depression and anxiety symptoms in people with cancer: A systematic review and meta-analysis. Psychooncology 2021, 30, 1196–1208.

27. Patsou, E.D.; Alexias, G.D.; Anagnostopoulos, F.G.; Karamouzis, M.V. Effects of physical activity on depressive symptoms during breast cancer survivorship: A meta-analysis of randomised control trials. ESMO Open 2017, 2, e000271.

28. Vashistha, V.; Singh, B.; Kaur, S.; Prokop, L.J.; Kaushik, D. The effects of exercise on fatigue, quality of life, and psychological function for men with prostate cancer: Systematic review and meta-analyses. Eur. Urol. Focus 2016, 2, 284–295.

29. Yi, L.J.; Tian, X.; Jin, Y.F.; Luo, M.J.; Jimenez-Herrera, M.F. Effects of yoga on health-related quality, physical health and psychological health in women with breast cancer receiving chemotherapy: A systematic review and meta-analysis. Ann. Palliat. Med. 2021, 10, 1961–1975.

30. Zabora, J.; BrintzenhofeSzoc, K.; Curbow, B.; Hooker, C.; Piantadosi, S. The prevalence of psychological distress by cancer site. Psychooncology 2001, 10, 19–28.

31. Albert, P.R. Why is depression more prevalent in women? J. Psychiatry Neurosci. 2015, 40, 219–221.

32. Vahdaninia, M.; Omidvari, S.; Montazeri, A. What do predict anxiety and depression in breast cancer patients? A follow-up study. Soc. Psychiatry Psychiatr. Epidemiol. 2010, 45, 355–361.

33. Ganz, P.A. Psychological and social aspects of breast cancer. Oncology 2008, 22, 642–650, discussion 650.

34. Baucom, D.H.; Porter, L.S.; Kirby, J.S.; Gremore, T.M.; Keefe, F.J. Psychosocial issues confronting young women with breast cancer. Breast Dis. 2005, 23, 103–113.

35. Helms, R.L.; O'Hea, E.L.; Corso, M. Body image issues in women with breast cancer. Psychol. Health Med. 2008, 13, 313–325.

36. Snoj, Z.; Akelj, M.P.; Lièina, M.; Pregelj, P. Psychosocial correlates of progesterone receptors in breast cancer. Depress. Anxiety 2009, 26, 544–549.
37. Kim, S.; Han, J.; Lee, M.Y.; Jang, M.K. The experience of cancer-related fatigue, exercise and exercise adherence among women breast cancer survivors: Insights from focus group interviews. J. Clin. Nurs. 2020, 29, 758–769.
38. Huang, H.P. The effect of a 12-week home-based walking program on reducing fatigue in women with breast cancer undergoing chemotherapy: A randomised controlled study. Int. J. Nurs. Stud. 2019, 99, 103376.
39. Schmitz, K.H.; Courneya, K.S.; Matthews, C.; Demark-Wahnefried, W.; Galvão, D.A.; Pinto, B.M. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. Med. Sci. Sports Exerc. 2010, 42, 1409–1426.
40. Kok, R.M.; Reynolds, C.F., 3rd. Management of depression in older adults: A review. JAMA 2017, 317, 2114–2122.
41. Loh, K.P.; Zittel, J.; Kadambi, S.; Pandya, C.; Xu, H.; Flannery, M.; Magnunson, A.; Bautista, J.; McHugh, C.; Mustian, K.; et al. Elucidating the associations between sleep disturbance and depression, fatigue, and pain in older adults with cancer. J. Geriatr. Oncol. 2018, 9, 464–468.
42. Loh, K.P.; Kleckner, I.R.; Lin, P.J.; Mohile, S.G.; Canin, B.E.; Flannery, M.A.; Fung, C.; Dunne, R.F.; Bautista, J.; Culakova, E.; et al. Effects of a home-based exercise program on anxiety and mood disturbances in older adults with cancer receiving chemotherapy. J. Am. Geriatr. Soc. 2019, 67, 1005–1011.
43. Gultyaeva, V.V.; Zinchenko, M.I.; Uryumtsev, D.Y.; Krivoschekov, S.G.; Aftanas, L.I. Exercise for depression treatment. Physiological mechanisms. Zh. Nevrol. Psikhiatr. SS Korsakova 2019, 119, 112–119.
44. Ruddy, K.J.; Stan, D.L.; Bhagra, A.; Jurisson, M.; Cheville, A.L. Alternative exercise traditions in cancer rehabilitation. Phys. Med. Rehabil. 2017, 28, 181–192.
45. Shea, B.J.; Grimshaw, J.M.; Wells, G.A.; Boers, M.; Andersson, N.; Hamel, C.; Porter, A.C.; Tugwell, P.; Moher, D.; Bouter, L.M. Development of AMSTAR: A measurement tool to assess the methodological quality of systematic reviews. BMC Med. Res. Methodol. 2007, 7, 10.
46. Scott, J.M.; Zabor, E.C.; Schwitzer, E.; Koelwyn, G.J.; Adams, S.C.; Nilsen, T.S.; Moskowitz, C.S.; Matsoukas, K.; IYengar, N.M.; Dang, C.T.; et al. Efficacy of exercise therapy on cardiorespiratory fitness in patients with cancer: A systematic review and meta-analysis. J. Clin. Oncol. 2018, 36, 2297–2305.
47. Gardner, J.R.; Livingston, P.M.; Fraser, S.F. Effects of exercise on treatment-related adverse effects for patients with prostate cancer receiving androgen-deprivation therapy: A systematic review. J. Clin. Oncol. 2014, 32, 335–346.
48. Winters-Stone, K.M.; Dobek, J.C.; Bennett, J.A.; Dieckmann, N.F.; Maddalozzo, G.F.; Ryan, C.W.; Beer, T.M. Resistance training reduces disability in prostate cancer survivors on androgen deprivation therapy: Evidence from a randomised controlled trial. Arch. Phys. Med. Rehabil. 2015, 96, 7–14.
49. Courneya, K.S.; Segal, R.J.; Mackey, J.R.; Gelmon, K.; Reid, R.D.; Friedenreich, C.M.; Ladha, A.B.; Proulx, C.; Vallance, J.K.H.; Lane, K.; et al. Effects of aerobic and resistance exercise in breast cancer patients receiving adjuvant chemotherapy: A multicenter randomised controlled trial. J. Clin. Oncol. 2007, 25, 4396–4404.
50. Kleckner, I.R.; Kamen, C.; Gewandter, J.S.; Mohile, N.A.; Heckler, C.E.; Culakova, E.; Fung, C.; Janlesins, M.C.; Asare, M.; Lin, P.; et al. Effects of exercise during chemotherapy on chemotherapy-induced peripheral neuropathy: A multicenter, randomised controlled trial. Support Care Cancer 2018, 26, 1019–1028.