European Review for Medical and Pharmacological Sciences 2023; 27: 8190-8197

Mindfulness-based stress reduction in cancer patients: impact on overall survival, quality of life and risk factor

P. FORTE[1], V. ABATE[1], I. BOLOGNINI[1], O. MAZZONI[1], V. QUAGLIARIELLO[2], N. MAUREA[2], D. DI BONITO[1], E. QUARATA[1], G. MIGLIACCIO[1], M. PETRILLO[1], D. BARBERIO[1]

[1]Oncologic Psychology, Istituto Nazionale Tumori – IRCCS-Fondazione G. Pascale, Naples, Italy
[2]Division of Cardiology, Istituto Nazionale Tumori – IRCCS-Fondazione G. Pascale, Naples, Italy

Abstract. **Mindfulness-based stress reduction, a complementary and alternative therapy, is able to decrease cancer-related fatigue, and stress and to improve the quality of life in cancer patients. Some studies evaluated if mindfulness-based stress reduction could improve some cardiometabolic and cancer risk factors, including systemic chemokines, growth factors, and pro-inflammatory biomarkers (e.g., C-reactive protein, Interleukin-1). In this narrative review, we highlight the pleiotropic beneficial effects of mindfulness-based stress reduction and its clinical impact on cardiovascular and cancer risk factors among patients with cancer in different stages. Moreover, improvements in the overall quality of life, sleep quality, and immune functions [changes in plasma levels of interleukin-4 (IL-4), interferon-γ (INF-γ), and interleukin-10 (IL-10)] will also be discussed. Albeit few clinical studies available in the literature, evidenced the beneficial effects of mindfulness-based stress reduction on the immune and cardiometabolic profile in cancer patients, providing important insights into the closest collaboration between psycho-oncologists, oncologists, and cardiologists.**

Key Words:
Psycology, Cancer, Inflammation, Mindfulness, Risk factors.

Introduction

Despite improvements in anticancer pharmacological therapies, cancer remained the second cause of death in the United States in 2020, after cardiovascular diseases[1]. Cancer patients experienced cancer-related and anticancer drug-related symptoms, ranging from pain, mucositis, cardiovascular diseases (i.e., heart failure, myocarditis), endocrine diseases, and others[2]. Moreover, cancer patients are exposed to a high risk of depression and fatigue after cancer diagnosis and therapies[3]. Recent data[4,5] described that cancer patients have a four times higher risk of depression than the general population. Unfortunately, only 25% of patients receive a formal diagnosis of depression. Therefore, the epidemiological data actually available in the literature should be underestimated[6]. Depression is associated with a high risk of mortality and a poor prognosis in patients with cancer. Therefore, clinical management of depression should be done in order to improve overall survival and quality of life (QoL)[7-9] (Figure 1).

Mindfulness-based interventions (MBI) have emerged as promising interventions for cancer-related distress and affective disorders[10], and the literature is full of research supporting MBIs in improving depressive symptoms, fatigue, and life expectancy in patients with cancer[11,12]. Some uncontrolled studies[13,14] have also demonstrated positive alterations in physical health indicators, such as immune functions and cortisol levels, as a result of mindfulness training. However, the effect of MBI on hormone secretion and potentially beneficial changes in the hypothalamic-pituitary-adrenal cortex axis (HPA) is still largely unknown. Cortisol levels have been found[15,16] to be linked to psychological well-being and seem, in particular, sensitive to negative emotional conditions. Dysregulation of the HPA axis and cortisol hormone levels have been reported[16,17] in cancer patients, especially a flattening of the circadian rhythm of cortisol secretion and high systemic levels of cortisol[18]. The clinical effects of HPA axis dysregulation in cancer patients are largely unknown[18]; however, one study[19] reported a significantly decreased survival among metastatic breast cancer patients with a flattened circadian rhythm of cortisol secretion. After analyzing the effects of

Corresponding Author: Pietro Forte, MD; e-mail: fortepietro19@gmail.com

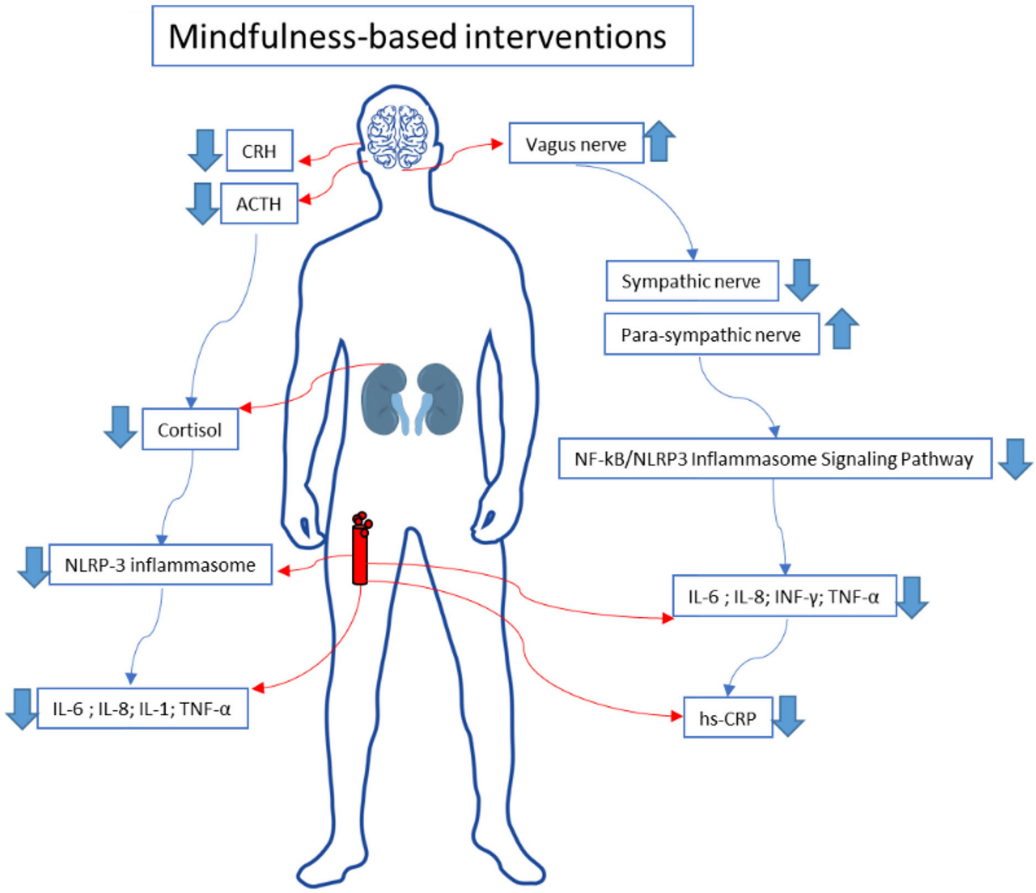

Figure 1. Main biochemical pathways of mindfulness-based interventions. In brief, mindfulness-based interventions decrease CRH-ACTH-Cortisol axis that reduces NLRP3 inflammasome activation in the body; a reduction in NLRP3 levels decreases systemic levels of IL-6, IL-1, IL-8, and TNF-α. On the other hand, mindfulness-based interventions increase vagus nerve, which reduces sympathetic activity in the autonomous nerve system; vagus nerve activation reduces NF-κB/NLRP3 inflammasome signaling pathway, determining anti-inflammatory systemic effects.

BMI on cancer patients, it was found that it could be clinically beneficial after three and six months. Specifically, after three months of MBI therapy, patients saw a reduction in Post Traumatic Stress Disorder (PTSD) symptoms and an improvement in their quality of life (QoL). As a secondary outcome of the study, salivary cortisol was determined before and during MBI in these patients; authors described that salivary cortisol has been shown to be a convenient and reliable way to measure cortisol levels and a good marker of HPA axis homeostasis.

Methods

A systematic search of the Medline and EMBASE databases was performed to identify all potentially relevant English-language scientific papers containing original articles on the effect of Mindfulness on cancer and cardiovascular diseases. The following search strings were used in PubMed: "Mindfulness OR Meditation AND cancer " OR "Mindfulness OR Meditation AND cortisol" OR "Mindfulness OR Meditation AND cardiovascular". The same research criteria were applied to Clinical Trial Register. The databases were last accessed on 28 February 2023.

Biochemical Effects of Mindfulness-Based Interventions: an Overview

Mindfulness-based interventions exert several beneficial effects on humans[20]. As summarized in Figure 1, mindfulness-based interventions reduce stress and systemic inflammation through many biochemical pathways. In summary, mindfulness-based interventions reduce the hypothalamic secretion of corticotropin-releasing hormone

(CRH), which in the pituitary gland inhibits adrenocorticotropic hormone (ACTH) synthesis and secretion[21]. Once in the circulation, lower levels of ACTH reduce cortisol secretion in adrenal glands, resulting in stress reduction inhibition of the NLR family pyrin domain containing 3 (NLRP-3) inflammasome levels (a key player in inflammation and cardiovascular disease[22]). Reduction of the NLRP3 inflammasome results in low levels of pro-inflammatory cytokines, such as interleukin-6 (IL-6), interleukin-8 (IL-8), interleukin-1 (IL-1) and tumor necrosis alpha (TNF-α)[23].

On the other hand, mindfulness-based interventions activate the vagus nerve[24]. Activation of the vagus nerve reduces sympathetic tone and activates parasympathetic tone in the autonomic nervous system[25]. Activation of the parasympathetic system results in suppressing the nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB)/NLRP3 inflammasome[26] signaling pathway, which reduces systemic levels of IL-6, IL-8, INF-γ, and TNF-α resulting in decreased hepatic synthesis of ultrasensitive C-reactive protein (hs-CRP)[27].

Cortisol Levels and Mindfulness-Based Interventions in Cancer Patients

Cancer patients experienced psychological stress at different levels before, during, and after cancer therapies, with significant changes in family relationships as well as in the daily management of life[28]. MBI is a complex of psychological interventions aimed at reducing stress and improving QoL in patients with acute and chronic diseases[29]. As summarized in Table I, recent meta-analyses[30,31] concluded that MBI is effective in reducing stress, cortisol levels, and depression as well as in improving QoL. Some uncontrolled studies[32,30] confirmed that MBI is able to reduce cortisol levels and improve immune functions in patients with and without cancer. Recent studies[33,34] in patients with type 2 diabetes and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection demonstrated that mindfulness-based stress reduction (MBSR) intervention significantly improved anxiety, depression, and stress, and reduced systemic cortisol levels.

Another recent study of 70 adult patients with low back pain demonstrated that 12 months of MBSR reduced systemic cortisol and Interleukin 1β (IL-1β) levels than the untreated group[35]. Moreover, MBSR reduced depression, stress, and perceived pain, improving general physical functions as well as sleep quality; the overall picture of this study indicates that MBSR could be an alternative and complementary medicine to improve pain and QoL in patients with low back pain[35]. A study in woman veterans at high risk of cardiovascular diseases concluded that MBSR decreased diurnal salivary cortisol and interleukin-6, indicating strong anti-inflammatory and potential cardioprotective effects of MBSR[36]. A randomized

Table I. Main clinical outcomes of mindfulness-based interventions in different populations.

Study (Ref)	Population	Clinical Outcomes
Grossman et al[30]	Healthy population	Reduction of stress, cortisol levels and depression. Improvement of QoL
Ledesma and Kumano[31]; Yuan et al[32]	Patients with and without cancer	Reduction of cortisol levels, Improvement of immune functions
Suh et al[33]; Sayadi et al[34]	Type 2 diabetes and SARS-CoV-2 infection	Reduction of anxiety, depression, stress, and reduction of systemic cortisol levels
Diez et al[35]	Healthy adult subjects	Reduction of systemic cortisol and Interleukin 1β (IL-1β) levels
Saban et al[36]	Woman veterans at high risk of cardiovascular diseases	Reduction of diurnal salivary cortisol and interleukin -6
Garland et al[37]	Cancer survivors	Reduction of systemic cortisol levels
Lipschitz et al[38]	Cancer survivors with sleep disturbance	Reduction in cortisol levels and sleep quality improvement
Matousek et al[39]	Breast cancer patients	Reduction of stress levels, depression, anxiety and pain
Duncan et al[40]	Breast cancer patients	Improvement of QoL and reduction of cortisol levels

controlled trial[37] with cancer survivors concluded that 4 and 12 weeks of the MBSR program could reduce systemic cortisol levels by promoting a pro-immune phenotype in these patients. Another pilot study[38] on fifty-seven cancer survivors with sleep disturbance described that MBSR is able to reduce cortisol levels slightly and improve sleep quality. Another study[39] in breast cancer patients demonstrated short-term effects of the MBSR program (three days); in brief, MBSR improved self-reported stress levels, depression, and some clinical symptoms, including anxiety and pain. A study[40] in prostate and breast cancer patients indicated that eight weeks of MBSR improved QoL and decreased stress symptoms, as well as reduced cortisol levels (Table I).

Mean Clinical Outcomes of Mindfulness-Based Stress Reduction Interventions in Cancer Patients

Mindfulness meditation interventions (MMBI) derived from MBSR techniques developed by Kabat-Zinn et al[41] in 1979. As summarized in Table II, the first clinical uses of MBSR were performed in debilitating patients with chronic pain and aimed to improve cognitive functions and reduce stress[41]. A pilot study[42] evaluated that MMBI is able to reduce cortisol levels and anxiety in advanced-stage cancer patients and also to improve QoL and quality of work in clinicians. A randomized controlled trial[43] in breast cancer patients assessed if MBSR could improve inflammation biomarker profile and immune functions. In detail, MBSR activates T cells through mitogen phytohemagglutinin and increases the Th1/Th2 ratio with a substantial recovery of B and Natural Killer cells, after cancer treatments[43]. The overall picture of the study indicates that MBSR could be able to change immune functions in patients with cancer and push attention to randomized trials in patients treated with Immune Checkpoint Inhibitors (ICIs)[43].

A study[44] on prostate and breast cancer patients indicates that twelve months of MBSR was effective in improving overall symptoms of stress as well as in reducing cortisol levels. Notably, Th1-related cytokines (with pro-inflammatory effects) and systolic blood pressure were strongly reduced in the MBSR group than in untreated patients, indicating anti-inflammatory and potential cardioprotective properties of MBSR in these patients[44] (Table II). A study[45] demonstrated that MBSR-based treatment improved symptoms of menopause and sleep quality in breast cancer patients. Another study[46] in patients with breast

Table II. Main clinical and cardiovascular outcomes of mindfulness-based stress reduction interventions in patients with/without cancer.

Study (Ref)	Population	Clinical Outcomes
Lengacher et al[42]	Advanced stage cancer patients	Reduction in cortisol levels, improvement in QoL and fatigue
Lengacher et al[43]	Breast cancer patients	Improvement of immune functions: increases in Th1/Th2 ratio; significant recovery of B and Natural Killer cells
Carlson et al[44]	Prostate and breast cancer patients	Improvement of stress; reduction in cortisol levels. Th1-related cytokines and systolic blood pressure were strongly reduced
Chang et al[45]	Breast cancer patients	Improvement in QoL, symptoms of menopause and sleep quality
Wu et al[46]	Breast cancer patients	Stress reduction, improvement in QoL and reduction of cancer-related fatigue
Lengacher et al[47]	Breast cancer patients	Reduction of IL-6 and cortisol levels
Zou et al[48]	Cancer survivors	Reduction of blood pressure
Helal et al[49]	Patients with heart failure	Reduction of hospitalization risk
Zou et al[50]	Patients with heart failure	Reduction of depression, anxiety and heart rate
Tulloh et al[51]	Patients with pulmonary arterial hypertension	Reduction of blood pressure and improvement of QoL
Joseph[53]	Patients with hypertension as well as chronic heart failure	Reduction of systolic and diastolic blood pressure
Norman et al[55]	Patients with chronic heart failure	Improvement of self-reported symptoms
Sullivan et al[56]	Patients with chronic heart failure	Reduction of anxiety and depression

cancer concluded that MBSR relieved psychological stress, reduced anxiety, and depression, and improved sleep quality, positioning itself as a non-pharmacological strategy effective to improve QoL in patients with cancer. A study[47] on 322 breast cancer patients demonstrated that six-week MBSR reduced cortisol and IL-6 levels. Cortisol levels were reduced immediately after the MBSR compared to baseline values; IL-6 changes had a similar behavior compared to cortisol, indicating the anti-inflammatory effects of MBSR in these patients[47].

Cardiovascular Outcomes of Mindfulness-Based Stress Reduction Interventions

As summarized in Figure 2, the MBSR program exerts some beneficial effects on patients with/without cancer. Among the improvement of QoL, stress, and reduction of cortisol levels in these patients, MBSR could be able to reduce cardiovascular risk factors. To date, few randomized clinical trials[48] have focused on the cardiovascular outcomes of MBSR, and none in the cancer patient cohort (Table II). However, some recent studies[48,49] indicate that MBSR could be beneficial to manage hypertension, and dyspnoea in chronic heart failure, and to reducing risk factors related to coronary heart disease, stroke, heart failure, aortic aneurysm, peripheral artery disease, and vascular dementia. A study[48] demonstrated that two months of MBSR is able to reduce blood pressure (systolic blood pressure decreased by 16 mmHg and diastolic blood pressure decreased by around 4 mmHg; $p<0.005$). A recent study[49] described that MBSR improved depression and QoL in patients with heart failure, and reduced hospitalization risk compared to untreated patients; however, the number of patients enrolled in this study is still to be improved, and large randomized controlled trials are needed to confirm these results. Another recent study[50] summarized that MBSR could be beneficial in patients with heart failure, by reducing depression, anxiety, and heart rate, however, also in this study, authors concluded that more controlled and rigorous studies are needed. An interesting study[51] aimed to verify the feasibility and the potential benefits of the MBSR program in patients with pulmonary arterial hypertension (PAH), considering its impact on reducing blood pressure and improving QoL. Authors[51,52] concluded that attendance at group MBSR was poor in people with chronic PAH;

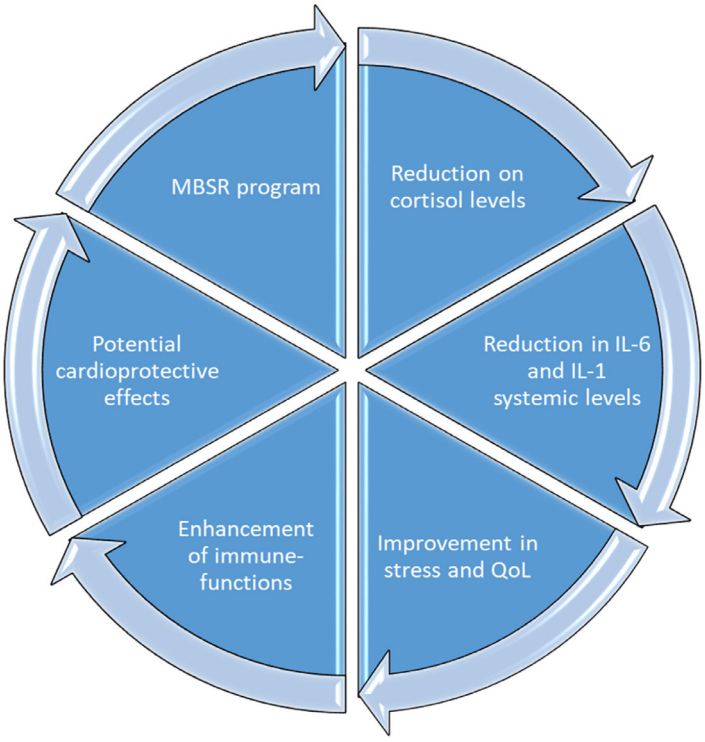

Figure 2. Main clinical outcomes of MBSR program in cancer patients. MBSR is able to reduce cortisol levels that consequently inhibit the synthesis of pro-inflammatory cytokines, e.g., IL-6 and IL-1. Cortisol reduction improves stress and QoL in these patients. The overall picture of the MBSR effects results in the enhancement of immune functions and reduction of cardiovascular and cancer-related risk factors

therefore, a proper MBSR program (*in situ* or through online programs) should be performed in these patients. Another study[53] demonstrated that MBSR significantly increases cardiac-vagal baroreflex sensitivity and heart-rate variability. These effects result in a significant reduction of systolic and diastolic blood pressure also in patients with hypertension as well as chronic heart failure[53].

In summary, MBSR could be cardioprotective due to its stimulation of the vagal system that reduces systemic inflammation through cholinergic anti-inflammatory pathways[54] (Table II) Another study[55] in stable but symptomatic outpatients with chronic heart failure, concluded that MBSR alleviated self-reported symptoms in addition to conventional treatment. However, the sample size is small in this study[55], and further studies are needed, but findings support the role of MBSR as a feasible method to reduce symptom burden in patients diagnosed with chronic heart failure. Another clinical trial[56] reported that eight weeks of MBSR reduced anxiety and depression in patients with chronic heart failure. Notably, MBSR improves symptoms of chronic heart failure after one year of treatment[56].

Conclusions

Randomized clinical trials available in the literature evidenced the beneficial effects of MBSR on the immune and metabolic functions of cancer patients, providing key insights into the closest collaboration between psycho-oncologists, oncologists, and cardiologists. As insight is gained into the clinical outcomes associated with MBSR methods, we propose MBSR as a complementary and alternative medicine warranting rapid investigation in patients with cancer, highlighting potential pro-immune and systemic anti-inflammatory outcomes.

Funding
This work was (partially) supported by the Italian Ministry of Health Ricerca 5x1000 "La Qualità di Vita nel paziente e nella sua famiglia: dallo spazio ludoteca all'utilizzo delle terapie non convenzionali". Funds, 2017.

Authors' Contributions
DB and NM conceived the manuscript, supervised the report and research, checked and validated the manuscript; VA, IB, OM and DDB contributed to the elaboration of literature and data; EQ, GM and MP supervised the paper; PF and VQ wrote, checked, revised and submitted the manuscript. All authors have read and agreed to the published version of the manuscript.

Ethics Approval
Not applicable.

Informed Consent
Not applicable.

Availability of Data and Materials
Not applicable.

Conflicts of Interest
The authors declare no conflict of interest.

ORCID ID
Daniela Barberio: 0000-0002-7722-2600

References

1) Ahmad FB, Cisewski JA, Minino A, Anderson RN. Provisional mortality data—United States, 2020. MMWR Morb Mortal Wkly Rep 2021; 70: 519-522.
2) Mundnich S, Saba MM. Cardio-Oncology in Chile: The Future of an Emerging Discipline. JACC CardioOncol 2022; 4: 555-558.
3) Park Y, Park K. Health-related quality of life and depressive symptoms of patients with chronic diseases and the general population before and during the COVID-19 pandemic in Korea. Front Psychol 2023; 14: 1117369.
4) Bortolato B, Hyphantis TN, Valpione S, Perini G, Maes M, Morris G, Kubera M, Köhler CA, Fernandes BS, Stubbs B, Pavlidis N, Carvalho AF. Depression in cancer: The many biobehavioral pathways driving tumor progression. Cancer Treat Rev 2017; 52: 58-70.
5) Aldea M, Craciun L, Tomuleasa C, Crivii C. The role of depression and neuroimmune axis in the prognosis of cancer patients. J BUON 2014; 19: 5-14.
6) Grassi L, Nanni MG, Rodin G, Li M, Caruso R. The use of antidepressants in oncology: a review and practical tips for oncologists. Ann Oncol 2018; 29: 101-111.
7) Álvarez-Pardo S, de Paz JA, Romero-Pérez EM, Tánori-Tapia JM, Rendón-Delcid PA, González-Bernal JJ, Fernández-Solana J, Simón-Vicente L, Mielgo-Ayuso J, González-Santos J. Related Factors with Depression and Anxiety in Mastectomized Women Breast Cancer Survivors. Int J Environ Res Public Health 2023; 20: 2881.
8) Pitman A, Suleman S, Hyde N, Hodgkiss A. Depression and anxiety in patients with cancer. BMJ 2018; 361: k1415.
9) Smith HR. Depression in cancer patients: pathogenesis, implications and treatment (review). Oncol Lett 2015; 9: 1509-1514.

10) Beshai S, Desjarlais SM, Green B. Perspectives of Indigenous University Students in Canada on Mindfulness-Based Interventions and their Adaptation to Reduce Depression and Anxiety Symptoms. Mindfulness (N Y) 2023; 14: 1-16.
11) Li J, Li C, Puts M, Wu YC, Lyu MM, Yuan B, Zhang JP. Effectiveness of mindfulness-based interventions on anxiety, depression, and fatigue in people with lung cancer: A systematic review and meta-analysis. Int J Nurs Stud 2023; 140: 104447.
12) Melis M, Schroyen G, Leenaerts N, Smeets A, Sunaert S, Van der Gucht K, Deprez S. The impact of mindfulness on cancer-related cognitive impairment in breast cancer survivors with cognitive complaints. Cancer 2023; 129: 1105-1116.
13) Carlson LE, Garland SN. Impact of mindfulness-based stress reduction (MBSR) on sleep, mood, stress and fatigue symptoms in cancer outpatients. Int J Behav Med 2005; 12: 278-285.
14) Carlson LE, Speca M, Patel KD, Goodey E. Mindfulness-based stress reduction in relation to quality of life, mood, symptoms of stress and levels of cortisol, dehydroepiandrosterone sulfate (DHEAS) and melatonin in breast and prostate cancer outpatients. Psychoneuroendocrinology 2004; 29: 448-474.
15) Lindfors P, Lundberg U. Is low cortisol release an indicator of positive health? Stress and Health 2002; 18: 153-160.
16) Raison CL, Miller AH. The neuroimmunology of stress and depression. Semin Clin Neuropsychiatry 2001; 6: 277-294.
17) Giese-Davis J, Wilhelm FH, Conrad A, Abercrombie HC, Sephton S, Yutsis M, Neri E, Taylor CB, Kraemer HC, Spiegel D. Depression and stress reactivity in metastatic breast cancer. Psychosom Med 2006; 68: 675-683.
18) McGregor BA, Antoni MH. Psychological intervention and health outcomes among women treated for breast cancer: a review of stress pathways and biological mediators. Brain Behav Immun 2009; 23: 159-166.
19) Sephton SE, Sapolsky RM, Kraemer HC, Spiegel D: Diurnal cortisol rhythm as a predictor of breast cancer survival. J Natl Cancer Inst 2000; 92: 994-1000.
20) Househam AM, Peterson CT, Mills PJ, Chopra D. The Effects of Stress and Meditation on the Immune System, Human Microbiota, and Epigenetics. Adv Mind Body Med 2017; 31: 10-25.
21) Turakitwanakan W, Mekseepralard C, Busarakumtragul P. Effects of mindfulness meditation on serum cortisol of medical students. J Med Assoc Thai 2013; 96 Suppl 1: S90-S95.
22) Quagliariello V, De Laurentiis M, Cocco S, Rea G, Bonelli A, Caronna A, Lombari MC, Conforti G, Berretta M, Botti G, Maurea N. NLRP3 as Putative Marker of Ipilimumab-Induced Cardiotoxicity in the Presence of Hyperglycemia in Estrogen-Responsive and Triple-Negative Breast Cancer Cells. Int J Mol Sci 2020; 21: 7802.
23) Leu SY, Tsang YL, Ho LC, Yang CC, Shao AN, Chang CY, Lin HK, Tsai PJ, Sung JM, Tsai YS. NLRP3 inflammasome activation, metabolic danger signals, and protein binding partners. J Endocrinol 2023; 257: e220184.
24) Guo HR, Wang JR, Wang YL, Huang BL, Yang XH, Ren YM. The effectiveness of mindfulness-based cognitive therapy combined with medication therapy in preventing recurrence of major depressive disorder in convalescent patients. Front Psychol 2022; 13: 882006.
25) Bonaz B, Sinniger V, Pellissier S. The Vagus Nerve in the Neuro-Immune Axis: Implications in the Pathology of the Gastrointestinal Tract. Front Immunol 2017 2; 8: 1452.
26) Black DS, Christodoulou G, Cole S. Mindfulness meditation and gene expression: a hypothesis-generating framework. Curr Opin Psychol 2019; 28: 302-306.
27) Fischer CP, Berntsen A, Perstrup LB, Eskildsen P, Pedersen BK. Plasma levels of interleukin-6 and C-reactive protein are associated with physical inactivity independent of obesity. Scand J Med Sci Sports 2007; 17: 580-587.
28) Okeke B, Hillmon C, Jones J, Obanigba G, Obi A, Nkansah M, Odiase N, Khanipov K, Okereke IC. The relationship of social determinants and distress in newly diagnosed cancer patients. Sci Rep 2023; 13: 2153.
29) Wan X, Huang H, Liang D, Jia RY, Chen CR. Effect of remote mindfulness-based interventions on symptoms of anxiety and depression in patients with chronic obstructive pulmonary disease: a protocol for systematic review and meta-analysis. BMJ Open 2022; 12: e055369.
30) Grossman P, Niemann L, Schmidt S, Walach H. Mindfulness-based stress reduction and health benefits. A meta-analysis. J Psychosom Res 2004; 57: 35-43.
31) Ledesma D, Kumano H. Mindfulness-based stress reduction and cancer: a meta-analysis. Psychooncology 2009; 18: 571-579.
32) Yuan Y, Lin L, Xie C, Lu Y, Liang J, Qi Y, Dong B, Chen Q, Fang Q, Tian L. Effectiveness comparisons of various psychosocial therapies for cancer-related fati gue: A Bayesian network meta-analysis. J Affect Disord 2022; 309: 471-481.
33) Suh HW, Jeong HY, Hong S, Kim JW, Yoon SW, Lee JY, Chung SY. The mindfulness-based stress reduction program for improving sleep quality in cancer survivors: A systematic review and meta-analysis. Complement Ther Med 2021; 57: 102667.
34) Sayadi AR, Seyed Bagheri SH, Khodadadi A, Jafari Torababadi R. The effect of mindfulness-based stress reduction (MBSR) training on serum cortisol levels, depression, stress, and anxiety in type 2 diabetic older adults during the COVID-19 outbreak. J Med Life 2022, 15: 1493-1501.
35) Diez GG, Anitua E, Castellanos N, Vázquez C, Galindo-Villardón P, Alkhraisat MH. The effect of mindfulness on the inflammatory, psychological and biomechanical domains of adult patients with low back pain: A randomized controlled clinical trial. PLoS One 2022; 17: e0276734.
36) Saban KL, Collins EG, Mathews HL, Bryant FB, Tell D, Gonzalez B, Bhoopalam S, Chroniak CP, Janusek LW. Impact of a Mindfulness-Based Stress Reduction Program on Psychological Well-Being, Cortisol, and Inflammation in Women Veterans. J Gen Intern Med 2022; 37: 751-761.

37) Garland EL, Beck AC, Lipschitz DL, Nakamura Y. Dispositional mindfulness predicts attenuated waking salivary cortisol levels in cancer survivors: a latent growth curve analysis. J Cancer Surviv 2015; 9: 215-222.
38) Lipschitz DL, Kuhn R, Kinney AY, Donaldson GW, Nakamura Y. Reduction in salivary α-amylase levels following a mind-body intervention in cancer survivors--an exploratory study. Psychoneuroendocrinology 2013; 38: 1521-1531.
39) Matousek RH, Pruessner JC, Dobkin PL. Changes in the cortisol awakening response (CAR) following participation in mindfulness-based stress reduction in women who completed treatment for breast cancer. Complement Ther Clin Pract 2011; 17: 65-70.
40) Duncan M, Moschopoulou E, Herrington E, Deane J, Roylance R, Jones L, Bourke L, Morgan A, Chalder T, Thaha MA, Taylor SC, Korszun A, White PD, Bhui K; SURECAN Investigators. Review of systematic reviews of non-pharmacological interventions to improve quality of life in cancer survivors. BMJ Open 2017; 7: e015860.
41) Kabat-Zinn J. Some reflections on the origins of MBSR, skillful means, and the trouble with maps. Contemp Buddhism 2011; 12: 281-306.
42) Lengacher CA, Kip KE, Barta M, Post-White J, Jacobsen PB, Groer M, Lehman B, Moscoso MS, Kadel R, Le N, Loftus L, Stevens CA, Malafa MP, Shelton MM. A pilot study evaluating the effect of mindfulness-based stress reduction on psychological status, physical status, salivary cortisol, and interleukin-6 among advanced-stage cancer patients and their caregivers. J Holist Nurs 2012; 30: 170-185.
43) Lengacher CA, Kip KE, Post-White J, Fitzgerald S, Newton C, Barta M, Jacobsen PB, Shelton MM, Moscoso M, Johnson-Mallard V, Harris E, Loftus L, Cox C, Le N, Goodman M, Djeu J, Widen RH, Bercu BB, Klein TW. Lymphocyte recovery after breast cancer treatment and mindfulness-based stress reduction (MBSR) therapy. Biol Res Nurs 2013; 15: 37-47.
44) Carlson LE, Speca M, Faris P, Patel KD. One year pre-post intervention follow-up of psychological, immune, endocrine and blood pressure outcomes of mindfulness-based stress reduction (MBSR) in breast and prostate cancer outpatients. Brain Behav Immun 2007; 21: 1038-1049.
45) Chang YC, Lin GM, Tseng TA, Vitale E, Yang CH, Yang YL. The Experience of Mindfulness-Based Stress Reduction on Menopausal Symptoms, Sleep Disturbance, and Body Image among Patients with Breast Cancer-A Qualitative Study. Curr Oncol 2023; 30: 1255-1266.
46) Wu H, Li F, Zhang F. The efficacy of mindfulness-based stress reduction vs. standard or usual care in patients with breast cancer: a systematic review and meta-analysis of randomized controlled trials. Transl Cancer Res 2022; 11: 4148-4158.
47) Lengacher CA, Reich RR, Paterson CL, Shelton M, Shivers S, Ramesar S, Pleasant ML, Budhrani-Shani P, Groer M, Post-White J, Johnson-Mallard V, Kane B, Cousin L, Moscoso MS, Romershausen TA, Park JY. A Large Randomized Trial: Effects of Mindfulness-Based Stress Reduction (MBSR) for Breast Cancer (BC) Survivors on Salivary Cortisol and IL-6. Biol Res Nurs 2019; 21: 39-49.
48) Zou L, Sasaki J, Wei GX. Effects of mind–body exercises (Tai Chi/Yoga) on heart rate variability parameters and perceived stress: a systematic review with meta-analysis of randomized controlled trials. J Clin Med 2018; 7: 404.
49) Helal SI, Lee G, Evans C, Grealish A. The Efficacy of Psychological Interventions on Health-Related Quality of Life for Patients With Heart Failure and Depression: A Systematic Review. J Cardiovasc Nurs 2022; 37: 134-145.
50) Zou H, Cao X, Geng J, Chair SY. Effects of mindfulness-based interventions on health-related outcomes for patients with heart failure: a systematic review. Eur J Cardiovasc Nurs 2020; 19: 44-54.
51) Tulloh RMR, Garratt V, Tagney J, Turner-Cobb J, Marques E, Greenwood R, Howard L, Gin-Sing W, Barton A, Ewings P, Craggs P, Hollingworth W. A pilot randomised controlled trial investigating a mindfulness-based stress reduction (MBSR) intervention in individuals with pulmonary arterial hypertension (PAH): the PATHWAYS study. Pilot Feasibility Stud 2018; 4: 78.
52) Tang YY. Short-term meditation training improves attention and self-regulation. Proc Natl Acad Sci USA 2007; 104: 17152-17156.
53) Joseph CN. Slow breathing improves arterial baroreflex sensitivity and decreases blood pressure in essential hypertension. Hypertension 2005; 46: 714-718.
54) Tracey KJ. The inflammatory reflex. Nature 2002; 420: 853-859.
55) Norman J, Fu M, Ekman I, Björck L, Falk K. Effects of a mindfulness-based intervention on symptoms and signs in chronic heart failure: A feasibility study. Eur J Cardiovasc Nurs 2018; 17: 54-65.
56) Sullivan MJ, Wood L, Terry J, Brantley J, Charles A, McGee V, Johnson D, Krucoff MW, Rosenberg B, Bosworth HB, Adams K, Cuffe MS. The Support, Education, and Research in Chronic Heart Failure Study (SEARCH): a mindfulness-based psychoeducational intervention improves depression and clinical symptoms in patients with chronic heart failure. Am Heart J 2009; 157: 84-90.