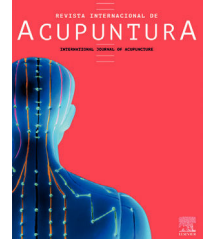




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REVIEW

Acupuncture and its potential in enhancing mental well-being for breast cancer survivors: An evidence-based insight

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Abstract Breast cancer survivors often face long-term physical and psychological challenges post-treatment, including anxiety, depression, sleep disturbances, and fatigue. Acupuncture, a traditional Chinese medicine technique, has shown promise in addressing these issues. This paper reviews several studies investigating the effects of acupuncture on the mental health of breast cancer survivors. A 15-year NADA auricular acupuncture service demonstrated improvements in mood, somatic symptoms, anxiety, and sleep problems, with benefits sustained at 4-week and 18-week follow-ups. Another study found auricular acupuncture to be superior to psychoeducation in improving sleep quality, stress, anxiety, and fatigue. Complementary acupuncture treatment significantly improved cancer-related fatigue, depression, and sleep quality. Additionally, electro-acupuncture outperformed gabapentin in improving sleep quality in breast cancer survivors with hot flashes. The reviewed studies employed various acupuncture techniques, including auricular and electro-acupuncture, with differences in treatment duration, frequency, and point selection. Mechanisms underlying acupuncture's effects on mental health remain complex and multifaceted, potentially involving modulation of neurotransmitter levels, neurotrophic factors, and pain pathways. However, the scarcity of high-quality randomized controlled trials and the lack of studies focusing specifically on mental health outcomes among breast cancer survivors highlight the need for further research in this area.

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PALABRAS CLAVE

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Acupuntura y su potencial Para mejorar el bienestar mental en sobrevivientes de cáncer de mama: Una perspectiva basada en la evidencia

Resumen Las sobrevivientes de cáncer de mama a menudo enfrentan desafíos físicos y psicológicos a largo plazo después del tratamiento, incluyendo ansiedad, depresión, trastornos del sueño y fatiga. La acupuntura, una técnica de medicina tradicional china, ha mostrado promesas en abordar estos problemas. Este artículo revisa varios estudios que investigan los efectos de la acupuntura en la salud mental de las sobrevivientes de cáncer de mama. Un servicio de acupuntura auricular NADA de 15 años demostró mejoras en el estado de ánimo, síntomas somáticos, ansiedad y problemas de sueño, con beneficios sostenidos en seguimientos de 4 semanas y 18 semanas. Otro estudio encontró que la acupuntura auricular fue superior a la psicoeducación en mejorar la calidad del sueño, el estrés, la ansiedad y la fatiga. El tratamiento complementario con acupuntura mejoró significativamente la fatiga relacionada con el cáncer, la depresión y la calidad del sueño. Además, la electroacupuntura superó a la gabapentina en mejorar la calidad del sueño en sobrevivientes de cáncer de mama con sofocos. Los estudios revisados emplearon diversas técnicas de acupuntura, incluyendo la auricular y la electroacupuntura, con diferencias en la duración del tratamiento, la frecuencia y la selección de puntos. Los mecanismos subyacentes de los efectos de la acupuntura en la salud mental siguen siendo complejos y multifacéticos, potencialmente implicando la modulación de los niveles de neurotransmisores, los factores neurotróficos y las vías del dolor. Sin embargo, la escasez de ensayos controlados aleatorizados de alta calidad y la falta de estudios centrados específicamente en los resultados de salud mental entre las sobrevivientes de cáncer de mama destacan la necesidad de más investigación en esta área.

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Introduction

According to the NIH's National Cancer Institute,¹ cancer is a condition characterized by uncontrolled growth and spread of abnormal cells within the body. These cells can originate from any part of the body, where they multiply and form tumors, which may be either cancerous (malignant) or non-cancerous (benign). Cancerous tumors have the ability to invade nearby tissues and can metastasize, spreading to distant parts of the body.

In 2022, there were a total of 19,976,499 reported cases of cancer globally, with 9,743,832 deaths.²

In particular, breast cancer is characterized by the uncontrolled growth of abnormal cells within the breast, forming tumors that have the potential to spread throughout the body if left untreated.³ While early-stage breast cancer (in situ) is not immediately life-threatening, invasive forms can spread to nearby tissues and organs, leading to the formation of tumors and potentially metastasizing to other parts of the body, which can be fatal.³ Treatment for breast cancer varies depending on factors such as the individual's health, the type of cancer, and its stage of progression, typically involving a combination of surgery, radiation therapy, and medication.⁴

Despite ranking fourth in mortality among all cancers in 2022 (669,846 deaths), breast cancer stands as the second most common cancer globally, following lung cancer, with a total of 2,310,051 reported cases.² However, by the end of 2020, there were approximately 7.8 million women alive who had been diagnosed with breast cancer within the past

five years, making it the most prevalent cancer globally.³ Breast cancer can occur in women of any age after puberty, with rates increasing in later life.^{3,5} Historically, breast cancer mortality remained relatively stable from the 1930s to the 1970s when surgery was the main treatment method. The advancements in survival rates began in the 1990s with the implementation of early detection programs linked to comprehensive treatment, including effective medical therapies that are constantly evolving.⁶⁻⁸

However, the post-treatment period marks a critical transition for individuals with breast cancer, as they shift from the role of "patients" to "survivors".⁹ The definition of breast cancer survivors has evolved over time. Initially, it denoted individuals who remained cancer-free for at least five years following diagnosis.¹⁰ However, this definition has expanded to include the period immediately post-treatment, encompassing those who are symptom-free or experience recurrence until the end of life.¹⁰ During this phase, survivors may face the risk of developing long-term physical and psychological complications stemming from the disease itself and its treatments, such as mastectomy, radiotherapy, and chemotherapy.¹¹ Regarding the psychological aspect, breast cancer survivors often are at risk of anxiety and depression,¹²⁻¹⁴ as well as sleep disturbances, **post-traumatic stress disorder (PTSD)**, somatisation, bipolar and obsessive-compulsive disorders, and even suicide.¹⁵

Therefore, it is imperative to prioritize mental health support for breast cancer survivors. Addressing psychological well-being is essential for optimizing the quality of

survivorship and enhancing overall outcomes for individuals overcoming breast cancer.

Acupuncture, a traditional Chinese medicine technique, is most accurately described as the precise insertion of fine needles into designated points along the meridians or channels of the body, through which qi, or life energy, is believed to flow.^{16,17} This practice targets the nervous, circulatory, endocrine, and exocrine systems, with the goal of fostering enhanced overall well-being.¹⁸ As an intervention, acupuncture therapy is often associated with improvements in anxiety,¹⁹ depression,²⁰ PTSD,²¹ among other psychological disorders.^{22–24}

According to Rodrigues et al.,²³ incorporating these practices into healthcare systems could offer therapeutic advantages for specific mental disorders and enhance the overall quality of life for patients with various medical conditions.

The primary aim of this study is to investigate the potential therapeutic effects of acupuncture on the mental health of individuals who have survived breast cancer. Additionally, we seek to explore the underlying mechanisms through which acupuncture may exert its influence in this context. Furthermore, we intend to analyze the methodologies employed in current research studies on acupuncture to provide a comprehensive understanding of its application in the field of breast cancer survivorship.

Acupuncture for mental health of breast cancer survivors

In this topic we report the main results of several studies that assessed variables that are related to mental health and wellbeing. **These results are summarized in Table 1.**

de Valois et al.²⁵ evaluated a 15-year NADA (National Acupuncture Detoxification Association) auricular acupuncture service for breast cancer survivors experiencing hot flashes and night sweats as a consequence of adjuvant hormonal therapies. In this study, data were analyzed from 415 referrals to a service offering patients eight NADA treatments. Results showed end-of-treatment improvements in several outcomes, of which including depressed mood, somatic symptoms, memory/concentration, anxiety/fears, and sleep problems. 4-week follow-up data showed that improvements were maintained for somatic symptoms, anxiety/fears, and sleep problems. However, only the benefits in anxiety/fears were maintained at the 18-week post-treatment follow-up assessment. Only two adverse events were reported. They were dizziness experienced at a first treatment, and dizziness and nausea on initial needling associated with an existing migraine.

A two-arm, single-centre, randomized controlled trial by Höttermann et al.²⁶ investigated the effect of auricular acupuncture and psychoeducation on sleep quality among 52 breast cancer survivors diagnosed with insomnia. Additionally, the study evaluated the effects of these interventions on inflammation markers (specifically IL-6), stress levels, anxiety, depressive symptoms, quality of life, fatigue, and the safety profile of both techniques. Auricular acupuncture significantly improved sleep quality, stress, anxiety, and fatigue at week 5 (end of intervention) compared to psychoeducation. However, the effect of both therapies

were similar for IL-6 levels, depressive symptoms, and quality of life. No significant group differences were observed at weeks 17 and 29 (follow-up) for any outcome. Adverse events were more common in the auricular acupuncture group, with the majority being non-serious and related to the intervention. Overall, auricular acupuncture demonstrated beneficial effects on sleep quality and psychological well-being in breast cancer survivors with insomnia. Those benefits were superior or equivalent to psychoeducation.

Another randomized controlled trial²⁷ explored the effect of an acupuncture intervention complementarily to psychological, nutritional, and exercise guidance on cancer-related fatigue of breast cancer survivors. Results demonstrated significant improvements in fatigue symptoms, serum hormone levels, and sleep quality following complementary acupuncture treatment. Specifically, breast cancer survivors receiving acupuncture exhibited notable improvements in general fatigue, physical fatigue, activity level, motivation, and mental fatigue compared to the control group not receiving acupuncture. Moreover, post-treatment serum levels of ghrelin, gastric inhibitory polypeptide, insulin, and leptin were significantly lower in the acupuncture group, indicating potential metabolic benefits. Additionally, improvements in sleep latency, hypnotic drug usage, and overall sleep quality were more pronounced in the acupuncture group. Important to the topic of this research, acupuncture also led to significant improvements in depression scores and quality of life compared to the control group. The authors report that no adverse events occurred during the trial. These findings suggest that acupuncture holds promise as a complementary therapeutic intervention for managing cancer-related fatigue, improving sleep quality and mental health among breast cancer survivors.

A pilot randomized controlled study by Smith et al.,²⁸ investigated the effect of acupuncture on post-cancer fatigue and well-being for women recovering from breast cancer. After 2 weeks, the acupuncture group participants showed a significant reduction in fatigue compared to the wait-list control. After 6 weeks, it was observed a significant improvement in well-being in the acupuncture group compared with the sham and wait list control. Relevant to the topic of this review, is the fact that the acupuncture group participants reported a positive intervention experience with well-being benefits possibly related to improvements in sleep, mood and relaxation. Despite not reporting adverse-effects, the authors highlight that the study demonstrated feasibility, good acceptability and treatment compliance with the study's interventions.

Studying the comparative effectiveness of electro-acupuncture vs. gabapentin medication for sleep disturbances in breast cancer survivors with hot flashes, Garland et al.²⁹ developed a 8-week randomized controlled trial with 58 participants. At the end of the 8-week treatment period, the electro-acupuncture group exhibited significantly greater improvements in the overall score of the Pittsburgh Sleep Quality Index compared to the gabapentin group. Furthermore, the electro-acupuncture group showed improvements in sleep latency and sleep efficiency compared to the gabapentin group. By Week 8, participants in the electro-acupuncture group reported improvements in

Table 1 Summary of the included studies.

Study	Improvements	P value
	End of treatment:	
de Valois et al. ²⁵	Depressed mood	0.0001
	Somatic symptoms	0.0001
	Memory/concentration	0.001
	Anxiety/fears	0.0001
	Sleep problems	0.0001
	4-week follow-up	
	Depressed mood	0.05
	Somatic symptoms	0.02
	Anxiety/fears	0.0001
	Sleep problems	0.0001
Höxtermann et al. ²⁶	18-week follow-up	
	Anxiety/fears	0.0001
	End of treatment: (compared to psychoeducation)	
	Sleep quality	0.031
	Stress	0.03
	Anxiety	0.001
	Fatigue	0.006
	End of treatment: (compared to the control group)	
	General fatigue	
	Motivation	
Li et al. ²⁷	Mental fatigue	
	Sleep latency	<0.01
	Hypnotic drug usage	
	Overall sleep quality	
	Depression scores	
	Quality of life	
	2 weeks of treatment: (compared to the wait-list control)	
	Fatigue	0.05
Smith et al. ²⁸	6 weeks of treatment: (compared with the sham and wait list control)	
	Well-being	0.006
	End of treatment: (compared to medication)	
	Sleep quality	0.044
	Sleep latency	0.041
	Sleep efficiency	0.05
	(compared to baseline)	
	Sleep duration	0.008
Garland et al. ²⁹	Sleep disturbance	0.032
	Sleep latency	0.025
	Daytime dysfunction	0.046
	Sleep efficiency	0.006
	Overall quality of sleep	0.008

various aspects of sleep, including duration, disturbance, latency, daytime dysfunction, efficiency, and overall quality compared to baseline. In contrast, the gabapentin group demonstrated improvements in sleep duration and quality only. Adverse effects were not reported. Overall, this study's results suggests that electro-acupuncture may be a good non-pharmacological option to address sleep disturbances in breast cancer survivors with hot flashes.

Acupuncture methodology

Overall, the analyzed studies employed several acupuncture techniques, including auricular acupuncture, acupuncture in

both standard and semi-standardized protocol form, and electro-acupuncture. Table 2 summarizes the characteristics of the studies included in this review.

While some studies adhere to standardized protocols targeting specific acupuncture points, others adopt semi-standardized or individualized approaches based on participant symptoms or TCM diagnosis. Evaluating the efficacy of these techniques requires considering factors such as treatment duration, frequency, needle retention time, and point selection, which may influence treatment outcomes and comparability between studies. Further research and standardization of acupuncture protocols are necessary to elucidate the most effective approaches for improving mental health outcomes among breast cancer survivors.

Table 2 Acupuncture methodology of the reviewed studies.

Study	Acupuncture methodology	Acupuncture points
de Valois et al. ²⁵	Auricular acupuncture Once a week for 8 weeks. 40 min. Needle retention.	Nada protocol: Auricular Sympathetic, Shenmen, Kidney, and Liver bilaterally, Upper Lung on the right ear, and Lower Lung on the left.
Höxtermann et al. ²⁶	Auricular acupuncture Twice a week for 5 weeks 20 min. Needle retention.	Semi-standardized protocol: Needles were placed in sensitive points (first on the postantitragal belt, second on the helix channel, and third on the shenmen). Additional points were used to address comorbid symptoms such as anxiety, hot flushes, and pain.
Li et al. ²⁷	Acupuncture Five times a week for 4 weeks. 30 min. Needle retention.	Standardized protocol: GV20 Bai hui, GV29 Yin tang, Li 3 Tai chōng, Li 4 Hegu, S 36 Zú sǎn lǐ, Sp 6 Sān yīn jiāo, and H 7 Shén mén.
Smith et al. ²⁸	Acupuncture Twice a week for 3 weeks, then once a week for 3 weeks. 20 min. Needle retention.	Semi-standardized protocol: Bilateral K 3 Tai xī, K 27 Shu fu, S 36 Zú sǎn lǐ and Sp 6 Sān yīn jiāo and CV 4 Guān yuán and CV 6 Qì hǎi.
Garland et al. ²⁹	Electro-acupuncture. Twice a week for 2 weeks, then once a week for 6 weeks. 30 min. Needle retention. 2 Hz pulse frequency.	Up to three secondary points (selection based on TCM differential diagnosis). Semi-standardized protocol: Not reported/found. Up to four secondary points (selection based on the participant's symptoms [e.g. fatigue, insomnia]).

However, and as mentioned in the work of Rodrigues et al.²³ and Simões et al.,³⁰ therapies utilizing Chinese medicine techniques such as acupuncture encompasses a dynamic process that requires constant adjustments and places significant emphasis on the unique characteristics of each patient. Consequently, they highlight a discrepancy between the treatment paradigms of Chinese and Western medicine, which leads to an underestimation of the efficacy of Chinese medicine techniques when subjected to evaluation through the scientific methodologies developed in the Western context.

Acupuncture mechanisms

Acupuncture, as any other therapy, may produce direct and indirect effects that reflect on the conditions being treated as well as in their comorbidities. The mechanisms through which acupuncture acts on the human being are still being studied to this date.^{21,31–34} In fact, this very topic is very complex and emerging evidence even suggests the existence of genetic predictors that determine the effectiveness of acupuncture treatment responses.³⁵

However, regarding the benefits reported above in this review, much should be discussed.

Approximately 40% to 70% of breast cancer survivors report experiencing sleep disturbances, persisting for years following their initial diagnosis.^{36–38} The implications caused by poor sleep quality and disrupted circadian rhythm are particularly serious in these cases due to its correlation with higher incidence of pathologies^{39–42} and therefore, higher chances for cancer recurrence.

All the studies analyzed in this review reported improvements on the sleep quality domain.

Some reported improvements in depression symptoms, mood, anxiety and stress, motivation, memory and mental fatigue.

Nowadays it is commonly accepted that psychological stress can be the root of many physical diseases.⁴³ Therefore and similar to what was stated regarding sleep, the implication of a poor mental health may undermine the overall wellbeing and recovery on breast cancer survivors.

Besides, on the field of mental health, comorbidity between conditions is very common.^{44,45} Developing each of the mentioned results could become redundant. Therefore, most of the acupuncture benefits on mental health symptoms may be related to the same or similar mechanisms.

For example, the study by Tu et al.⁴⁶ suggests that acupuncture may modulate glutamate receptors and excitatory amino acid transporters. The disruption of these receptors and transporters may be associated with depression,⁴⁷ bipolar disorder,⁴⁸ anxiety,⁴⁹ Parkinson's⁵⁰ among others.⁵¹ Therefore, if acupuncture is able to modulate glutamate receptors, it may assist in managing several diagnostically different conditions.

In addition, prior research had already elucidated the neuroprotective properties and neurotransmitter regulatory effects of acupuncture therapy.⁵²

In that line of thought, the influence of acupuncture on the Brain-derived neurotrophic factor (BDNF) has been studied.^{53–55} BDNF is a neurotrophin that is crucial to the survival, growth, and maintenance of neurons in vital brain circuits involved in emotional and cognitive function.^{56,57} Since acupuncture benefits the central nervous system through the modulation of BDNF signaling pathways,⁵⁸ it is possible that acupuncture can have a positive impact on the mental health of breast cancer survivors through this same mechanism.

Furthermore, acupuncture has been demonstrated to enhance 5-HT (serotonin) and DA (dopamine) levels in rat models of depression.⁵⁹ Alterations in neurotransmitter levels such as DA and 5-HT in various brain regions contribute

to neuropsychiatric, autonomic nervous system, and sleep disorders.^{60–64}

In fact, multiple studies have reported that acupuncture modulated 5-HT expression levels in various locations, including the serum, hypothalamus, and hippocampus.^{65–68} As well, DA expression levels were also modulated by acupuncture,^{66–69} possibly through the regulation of the ventral tegmental area-nucleus accumbens DA pathway.⁷⁰ DA related neurons are primarily located in the midbrain, particularly in the ventral tegmental area.^{71,72}

However, there is one more factor that should be acknowledged in this topic.

Breast cancer treatments may impose several side effects, among the most common, impaired function and pain.^{73–75} In fact, there seems to exist a bidirectional relation between mood/sleep disorders and pain.^{76–79} In this perspective, we can also highlight the influence that improving mood and sleep may assist in improving pain in breast cancer survivors, suggesting that the opposite may also occur. Acupuncture is commonly associated with improvements in pain^{80–82} and therefore, indirectly resulting in improved mood.

Electroacupuncture for instance, achieves pain relief by triggering various bioactive chemicals through peripheral, spinal, and supraspinal pathways. These chemicals include opioids, which desensitize peripheral pain receptors and reduce pro-inflammatory cytokines, as well as 5-HT and NE (norepinephrine), which decrease the phosphorylation of the spinal NMDA (N-methyl-D-aspartate) receptor subunit GluN1.⁸² However, the complexity of the mechanisms are not in the scope of this review. These mechanisms may also vary according to patient specific characteristics and other variables such as acupuncture points.^{31,83}

Final remarks

The studies reviewed provide some insights into the potential benefits of acupuncture for improving the mental health and overall well-being of breast cancer survivors. Across the studies, acupuncture demonstrated promising results in alleviating symptoms such as depressed mood, anxiety, stress, fatigue, and sleep disturbances commonly experienced by this population.

Additionally, while acupuncture showed significant improvements in various mental health parameters, the underlying mechanisms remain complex and multifaceted. Emerging evidence suggests that acupuncture may modulate neurotransmitter levels, neurotrophic factors, and pain pathways, contributing to its therapeutic effects. Further research is needed to elucidate these mechanisms comprehensively and their specific implications for mental health outcomes in breast cancer survivors.

Limitations

A specific limitation found in our research was the lack of high quality studies with only a few randomized controlled studies available. However, the limitation that is mostly noted is the lack of studies focusing specifically on mental health in this population. Our results report mainly secondary outcomes present in these studies.

In addition, the methodologies employed varied among the studies, ranging from auricular acupuncture to electro-acupuncture, with differences in treatment frequency, duration, and point selection.

Furthermore, several other limitations should be acknowledged regarding general research and access to acupuncture treatment. According to the results of the study of Bao et al.,⁸⁴ breast cancer survivors may encounter several barriers regarding the use of acupuncture. Common barriers include limited knowledge about acupuncture, concerns regarding insurance coverage and associated costs, and difficulty in locating qualified acupuncturists. In addition, minority patients and individuals with lower levels of education reported heightened perceived barriers compared to their white counterparts and those with higher education. Addressing these barriers, particularly through education initiatives and improvements in insurance coverage, holds promise for expanding access to acupuncture treatment among breast cancer survivors from diverse demographic backgrounds.

Future research directions

The scarcity of high-quality studies, particularly randomized controlled trials, underscores the need for more robust research methodologies to assess the efficacy of acupuncture in addressing the needs of breast cancer survivors. Rigorous randomized controlled trial can provide stronger evidence regarding the effectiveness of acupuncture interventions and help elucidate its impact on various outcomes, including mental health.

As mentioned before, there is a notable gap in the literature regarding studies specifically focusing on mental health outcomes among breast cancer survivors undergoing acupuncture treatment. Future research should prioritize investigating the effects of acupuncture on mental health parameters such as anxiety, depression, and overall psychological well-being. This could involve designing studies with mental health outcomes as primary endpoints to provide more comprehensive insights into the therapeutic potential of acupuncture in this population.

Building upon the previous barriers, future research efforts should delve deeper into understanding and mitigating factors that affects breast cancer survivors' access to acupuncture. This could involve more qualitative research to explore the underlying reasons behind limited knowledge, concerns about insurance coverage and costs, and difficulties in finding qualified practitioners. Additionally, interventions aimed at improving education, increasing awareness, and enhancing insurance coverage could be valuable for in reducing barriers and expanding access to acupuncture treatment.

As well, recognizing disparities in perceived barriers among minority patients and those with lower education levels is crucial. Future studies should strive to ensure diverse demographic representation. By including a more representative sample of breast cancer survivors, researchers can better understand how barriers to acupuncture use vary across different demographic groups and tailor interventions accordingly.

Conclusions

Acupuncture is a promising complementary therapeutic intervention that may provide assistance in managing mental health symptoms and improving overall quality of life among breast cancer survivors. However, continued research efforts are needed to refine treatment approaches, enhance understanding of underlying mechanisms, and address barriers to access, ultimately optimizing the effectiveness of acupuncture in supporting the mental well-being of this population.

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Ethical approval

This review does not require ethical approval.

Declarations of interest

None.

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