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Article

Effects of Wu's Long-Snake-Like Moxibustion on post-stroke cancer patients

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Abstract: Background: Due to the combined effects of stroke and cancer treatment, post-stroke cancer patients face the multiple burdens of psychological distress, sleep disorders, and declined quality of life. Wu's Long-Snake-Like Moxibustion, a therapeutic approach combining traditional Chinese medicine and modern medical concepts, aims to alleviate these challenges by regulating qi and blood through acupoint stimulation. This study explored the effects of Wu's Long-Snake-Like Moxibustion on psychological distress, sleep disorders, and quality of life in post-stroke cancer patients, with a specific focus on hypertension as a comorbidity. **Methods:** A case-control study recruited 60 participants who were assigned to either the treatment group (Wu's Long-Snake-Like Moxibustion) or the control group (standard care). Psychological distress, sleep quality, and quality of life were assessed using standardized scales, including the Hospital Anxiety and Depression Scale (HADS), Generalized Anxiety Disorder-7 (GAD-7), Pittsburgh Sleep Quality Index (PSQI), and European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30). Blood pressure was measured at baseline and at 12 weeks. Paired t-tests were used for intra-group comparisons, and independent *t*-tests were applied for inter-group differences. **Results:** At 12 weeks, the treatment group showed significant improvements on all measures. Anxiety (HADS-A) decreased from 14.2 (SD = 3.4) to 5.1 (SD = 2.0) (p = 0.02), and sleep quality (PSQI) improved from 8.7 (SD = 2.3) to 3.2 (SD = 1.6) ($p < 0.0001$). Quality of life, including physical (from 57.3 to 85.4) and emotional (from 45.8 to 80.1), significantly improved (p = 0.01 and p = 0.002, respectively). Blood pressure reductions in the treatment group were also significant, with systolic pressure dropping from 142.3 (SD = 12.5) to 118.6 (SD = 8.9) (p = 0.001). In contrast, the control group showed modest improvements in anxiety (from 13.9 to 10.4), sleep quality (from 8.3 to 6.7), and blood pressure (from 140.8 to 133.2). **Conclusion:** Wu's Long-Snake-Like Moxibustion not only significantly improved the psychological distress, sleep quality, and quality of life of post-stroke cancer patients but also effectively reduced hypertension. These findings suggest that Wu's Long-Snake-Like Moxibustion may be an effective complementary therapy for managing the complex needs of this patient population.

Keywords: Wu's Long-Snake-Like Moxibustion; stroke; cancer patients; psychological distress; sleep disorders; quality of life; hypertension

1. Introduction

Stroke and cancer are among the most prevalent diseases that cripple patients, especially when they occur simultaneously. Stroke often results in severe physical disabilities, cognitive impairments, and emotional disturbances that continue to affect the patient's functional level and quality of life [1]. At the same time, cancer patients face a complex interplay of psychological, physical, and emotional pressures associated with disease progression, side effects of treatment, and stress associated

with managing severe long-term health complications [2]. The coexistence of stroke and cancer exacerbates the physical and psychological burden on patients. These patients frequently experience a series of challenges, such as not only the obstacles caused by stroke but also the emotional, cognitive, and physical effects of cancer treatment, which overall worsen their condition [3].

The post-stroke patient with cancer often experiences deep, complex psychological disorders, including intensified anxiety, depression, and fear. Cancer itself can create a state of anxiety as patients worry about their disease progression, the effectiveness of treatment, and overall prognosis [4,5]. Simultaneously, stroke survivors experience the emotional impact of their physical disabilities, speech disorders, and social isolation, which exacerbates their suffering [6]. The double burden of having cancer or a stroke typically puts patients into a continuous condition of greater susceptibility, perpetuating a cycle wherein psychological misery heightens physical expressions of each disease, thus becoming an endless medical downhill spiral of sorts [7].

A serious factor aggravating the state of post-stroke cancer patients is sleep disorders. Sleep disorders are common in stroke and cancer patients, including insomnia, fragmented sleep, and poor sleep quality. Pain, anxiety, depression, and adverse reactions to cancer treatments are some of the factors that aggravate sleep problems [8,9]. This lack of sleep can have a ripple effect on recovery, immunity, and overall health. Poor sleep can also affect the rehabilitation outcomes of stroke patients, while in cancer patients, inadequate rest can impair the body's ability to fight infections and manage treatment side effects [10]. Therefore, improving sleep quality is of paramount importance for promoting recovery and enhancing the health of patients.

The quality of life (QoL) is often significantly impaired in post-stroke cancer patients. QoL includes several elements, such as physical health, psychological state, social relationships, and environmental factors [11]. In this group of patients, the physical disability caused by stroke, the suppressive effect of cancer treatment, and the emotional load of both diseases led to a reduced QoL. It improves the QoL not only in the context of reducing pain and fatigue but also by enhancing mental health, restoring social function, and improving daily living ability [12,13]. Hence, treatment targeting the physical and psychological aspects of their lives is highly valuable.

Another major issue associated with stroke and cancer patients is hypertension, which is often a complicating factor in the overall health management of these patients. Chronic hypertension could exacerbate stroke-related impairments and interfere with the effectiveness of cancer treatment [11]. The patient may have an increased risk of additional strokes, further impairing his physical capabilities and complicating recovery efforts. Further, hypertension is related to poorer prognosis in cancer patients, as it may affect organ function, increase the probability of cardiovascular complications, and hinder the body's ability to cope with the stress of cancer treatment [13]. Therefore, controlling hypertension is essential for improving overall health and improving the effectiveness of stroke and cancer treatments.

Wu's Long-Snake-Like Moxibustion is a novel therapeutic method that integrates traditional Chinese moxibustion techniques with modern medical concepts. Its purpose is to regulate the balance of qi and blood in the body, promote self-healing,

and improve various physiological and pathological conditions [14]. This approach has shown promising effects, particularly in managing chronic conditions such as pain and emotional distress. Research shows that moxibustion can improve the postoperative symptoms of breast cancer patients, such as fatigue, anxiety, and depression [15]. Moxibustion may be an effective intervention for post-stroke depression, insomnia, and cognitive impairment [16–18]. Wu's Long-Snake-Like Moxibustion targets specific acupuncture points and meridians that stimulate the body's natural healing mechanisms and may provide comprehensive treatment for the complex needs of post-stroke cancer patients [19]. In this regard, Wu's Long-Snake-Like Moxibustion offers a potential non-pharmacological treatment for this patient population, which would address not only the symptoms of psychological distress but also sleep disorders, quality of life, and hypertension [20].

The purpose of this study was to investigate the effects of Wu's Long-Snake-Like Moxibustion on psychological distress, sleep disorders, and quality of life in post-stroke cancer patients. In addition, it also explored the possible regulatory mechanism of hypertension in this treatment process, examining whether Wu's Long-Snake-Like Moxibustion can improve the physical and mental health of these patients by regulating blood pressure.

2. Materials and methods

2.1. Study design

In this study, a case-control design was used to evaluate the psychological distress, sleep disorders, quality of life, and hypertension regulation in post-stroke cancer patients treated with Wu's Long-Snake-Like Moxibustion. The trial compared the treatment outcomes of patients receiving Wu's Long-Snake-Like Moxibustion with the control group receiving standard care. This study was conducted at a tertiary care center specializing in stroke and cancer rehabilitation. It followed a double-blind procedure for outcome assessments, which would ensure objectivity and reliability in the assessment of treatment effects. The duration of the trial was 12 weeks, with follow-up assessments at 4, 8, and 12 weeks to monitor immediate and longer-term effects.

2.2. Participant selection

Participants were recruited from the stroke and cancer rehabilitation wards of the hospital. Inclusion criteria included: (1) Adults aged 18–75 years; (2) diagnosis of both stroke (at least 3 months after the stroke) and cancer (ongoing or completed treatment within the last 2 years); (3) evidence of psychological distress, sleep disturbances, and/or hypertension; and (4) the ability to provide written informed consent. The exclusion criteria were: (1) Active stroke or cancer recurrence during the study period; (2) severe cognitive impairment or inability to understand the treatment protocol; (3) contraindications to moxibustion therapy; and (4) pregnancy. A total of 60 participants were recruited, including 30 in the treatment group (Wu's Long-Snake-Like Moxibustion) and 30 in the control group.

2.3. Intervention

The treatment group adopted Wu's Long-Snake-Like Moxibustion therapy, which combined traditional Chinese moxibustion techniques with modern medical concepts. The stimulation of specific acupoints by moxibustion and acupuncture needles is part of this therapy. The targets are basically related to regulation of qi and blood, such as emotional regulation, pain management, and balance of energy in general. It was administered twice a week for 12 weeks, lasting about 30–45 min each time. These involve acupoints associated with Heart, Liver, Kidney, and Spleen meridian, as well as several other acupoints used for managing emotions and controlling blood pressure. Moxibustion was performed by placing the heat of the moxa stick close to the acupoints so that the level of heat provided to the acupoints does not exceed any limit to the effective body healing response. The practitioner responsible for treatment included qualified traditional Chinese medicine practitioners with rich exposure to moxibustion.

The control group received routine medical care, mainly including medication treatment for psychological distress symptoms, such as antidepressants or anxiolytic drugs, and treatment of hypertension through the intake of antihypertensive medications, in addition to basic rehabilitation for stroke. The control group did not receive moxibustion treatment, but it was recommended to make regular appointments with the doctors and follow treatment instructions.

2.4. Outcome measures

The impact of Wu's Long-Snake-Like Moxibustion on the subjects was assessed using different outcome measures as mentioned below:

- Psychological distress: The primary outcome of psychological distress was measured by the Hospital Anxiety and Depression Scale (HADS). This scale monitors the severity of symptoms of anxiety and depression. In addition, at baseline and at weeks 4, 8, and 12, depressive symptoms and anxiety level were assessed by the Patient Health Questionnaire-9 (PHQ-9) and the Generalized Anxiety Disorder-7 (GAD-7), respectively.
- Sleep disorders: The Pittsburgh Sleep Quality Index (PSQI) was utilized to assess sleep quality, including latency, duration, and disturbances in sleep. In addition, the Epworth Sleepiness Scale (ESS) was administered to evaluate daytime sleepiness and overall sleepiness during normal activities. All these measurements were taken at baseline and at 4, 8, and 12 weeks.
- Quality of life: The quality of life was evaluated with the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30). The tool aims to evaluate the overall quality of life through aspects of physical function, emotional functioning, social functioning, and pain. Administration was on all study entry visits as well as during the 4, 8, and 12 weeks of follow-up.
- Hypertension: Sphygmomanometry was used to measure the blood pressure levels at baseline and at each follow-up at weeks 4, 8, and 12. The systolic and diastolic blood pressure values were recorded. Then, the effect of moxibustion on blood pressure was analyzed by comparing the changes in blood pressure between the intervention group and the control group.

2.5. Statistical analysis

All analyses were conducted with Statistical Package for the Social Sciences (SPSS) version 26.0 for Windows. Baseline characteristics and outcome measurements were analyzed by descriptive statistics, expressed as mean ± standard deviation. The paired *t*-test was used to compare the scores of each group before and after treatment, in order to assess changes within the group. Independent *t*-tests or non-parametric tests were used to compare differences between groups. The significance level was set at a *p*-value less than 0.05. The multivariate analysis was done in order to account for confounding factors such as age, gender, and baseline comorbidities. All the analyses were conducted using an intention-to-treat approach to reduce bias.

2.6. Ethical considerations

This study has been approved by the Institutional Review Board (IRB). All participants provided written informed consent prior to enrollment to ensure they understood the study procedures, potential risks, and benefits. Ethical guidelines were followed throughout the study, including the confidentiality of participants and the voluntary nature of participation. Participants in the treatment group were informed that they could withdraw from the study at any time without affecting their medical care.

3. Results

Firstly, we analyzed the demographic characteristics of the treatment and control groups (**Table 1**). There were no significant differences in age, weight, height, and gender distribution between the two groups ($p > 0.05$). The mean age of participants in the treatment group was 63.5 years ($SD = 7.2$), and the control group was 62.8 years ($SD = 6.9$), with no statistical difference between the two groups ($p = 0.62$). The two groups achieved good balance in terms of gender ($p = 0.68$). The number of hypertensive individuals, as well as the number of patients with various types of cancer reported, was also well balanced between the two groups ($p > 0.05$). The absence of significant demographic differences further supports the validity of the comparative analysis between the treatment and control groups.

Table 1. The demographic characteristics of the treatment and control groups.

Variable	Treatment Group ($n = 30$) Mean	Treatment Group ($n = 30$) SD	Control Group ($n = 30$) Mean	Control Group ($n = 30$) SD	*P*-Value (Treatment vs. Control)
Age (Years)	63.5	7.2	62.8	6.9	0.62
Gender (Male)	15		14		0.68
Gender (Female)	15		16		0.68
Baseline Weight (kg)	68.2	12.3	69.1	11.8	0.45
Baseline Height (cm)	168.4	6.1	167.8	5.9	0.76
Hypertension (Yes)	18		20		0.59
Cancer Type (Lung)	8		10		0.68
Cancer Type (Breast)	7		9		0.76
Stroke Type (Ischemic)	20		21		0.73
Stroke Type (Hemorrhagic)	10		9		0.8

In terms of psychological distress, the baseline HADS-A (anxiety) mean score was higher in the treatment group (*M* = 14.2, *SD* = 3.4) and was not significantly different from the mean score in the control group (*M* = 13.9, *SD* = 3.6, **Figure 1**). The anxiety of the treatment group significantly decreased in anxiety over the 12-week period, with the mean HADS-A score decreasing to 5.1 (*SD* = 2.0), indicating a significant improvement compared to the baseline ($p = 0.02$). The control group only showed a modest reduction to 10.4 (*SD* = 3.0) ($p = 0.04$). The results of this part showed that Wu's Long-Snake-Like Moxibustion can effectively alleviate psychological distress compared to standard care.

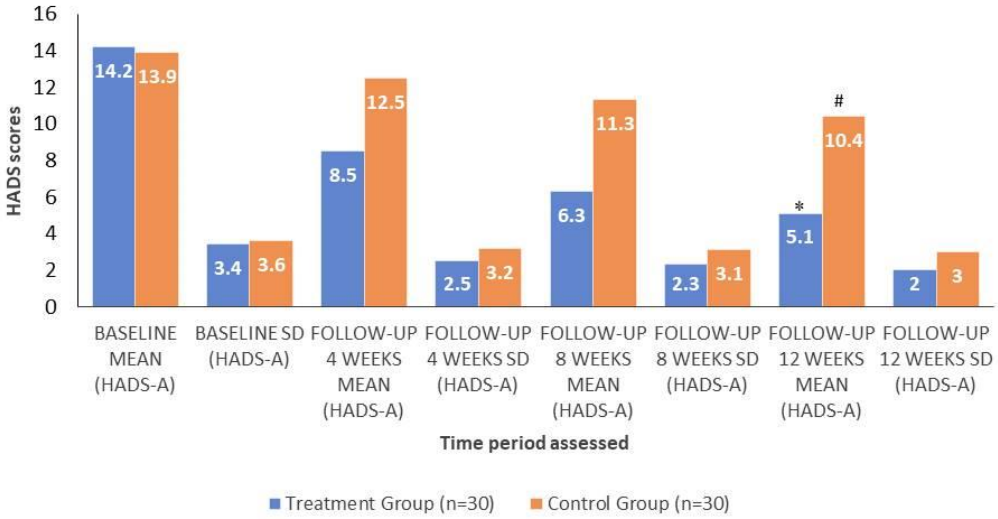

Figure 1. HADS scores assessed across the included participants.

Note: Compared with baseline of treatment group $^{*}p < 0.05$. Compared with baseline of control group $^{\#}p < 0.05$.

The GAD-7 score was used to measure anxiety symptoms. Baseline: The mean score of the treatment group was 15.0 (*SD* = 4.2) at baseline, and the control group had a similar mean score of 14.7 (*SD* = 4.5, **Figure 2**). By 12-week follow-up, the treatment group's mean GAD-7 score dramatically declined to 5.3 (*SD* = 2.8, $p = 0.01$, **Figure 2**), indicating great improvement in anxiety level. The control group showed improvement at 12 weeks with a score of 11.1 (*SD* = 3.8, $p = 0.03$, **Figure 2**). The decrease in GAD-7 score once again highlighted the greater role of Wu's Long-Snake-Like Moxibustion in relieving anxiety.

Next, the PSQI was applied to evaluate the effect of Wu's Long-Snake-Like Moxibustion on overall sleep quality. At the baseline, the mean PSQI score was reported to be 8.7 (*SD* = 2.3, **Figure 3**) among the treatment groups and 8.3 among the control group (*SD* = 2.5, **Figure 3**). After 12 weeks, the sleep quality of the treatment group improved significantly, with the PSQI score dropping to 3.2 (*SD* = 1.6, $p < 0.0001$, **Figure 3**). The control group only reduced to 6.7 (*SD* = 1.8, $p = 0.05$, **Figure 3**). The results indicated that Wu's Long-Snake-Like Moxibustion had a more pronounced effect on improving sleep quality compared to standard care.

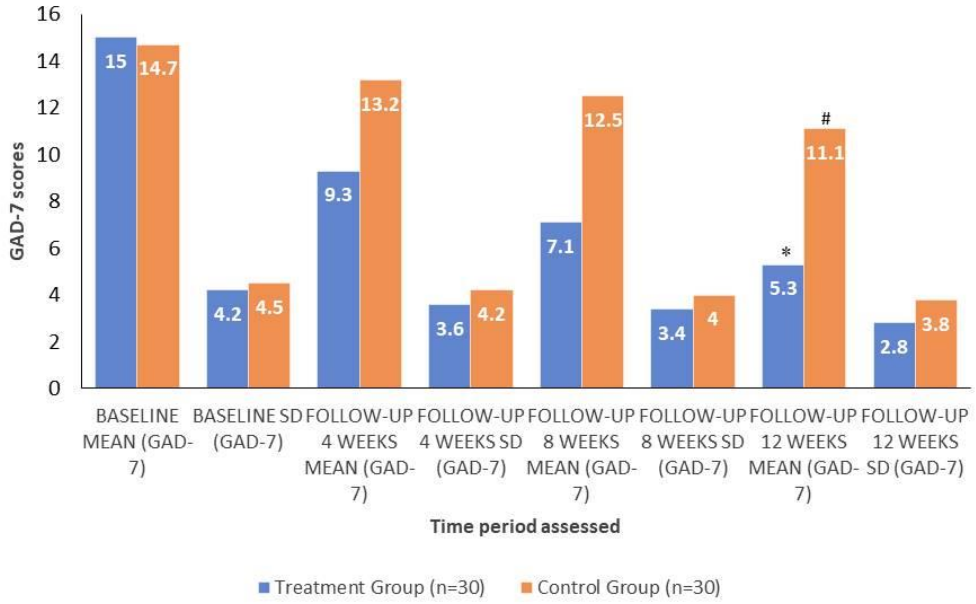

Figure 2. GAD-7 scores assessed across the included participants.

Note: Compared with baseline of treatment group $^{*}p < 0.05$. Compared with baseline of control group $^{\#}p < 0.05$.

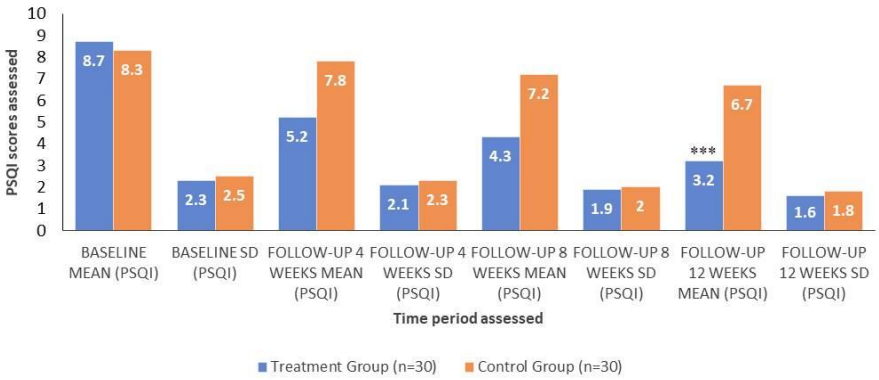

Figure 3. Pittsburgh Sleep Quality Index (PSQI) scores assessed.

Note: Compared with baseline of treatment group $^{***}p < 0.05$.

The physical functioning was evaluated by the EORTC QLQ-C30 scores. The baseline mean values for the treatment group and the control group were 57.3 (SD = 10.5) and 56.5 (SD = 10.8), respectively. After 12 weeks, the treatment group showed a significant improvement in physical functioning, with the mean score rising to 85.4 (*SD* = 6.3, *p* = 0.01, **Figure 4**), while the control group's score increased to 75.3 (*SD* = 7.2, *p* = 0.04, **Figure 4**). These results indicated that the treatment group experienced more notable improvements in physical health and daily functioning.

For the EORTC QLQ-C30 (**Figure 5**), the treatment group attained a mean of 45.8 (*SD* = 12.2) at baseline. In the control group, the mean was 46.5 (*SD* = 13.1). During the 12-week study period, the average score in the treatment group was impressive as the average score in emotional health improved highly, eventually reaching a mean score of 80.1 (*SD* =7.3, *p* = 0.002). On the other hand, the score of emotional functioning in the control group increased to 65.4 (*SD* = 8.2, *p* = 0.05). Data

analysis showed that Wu's Long-Snake-Like Moxibustion had a greater impact on the emotional regulation and psychological health of post-stroke cancer patients.

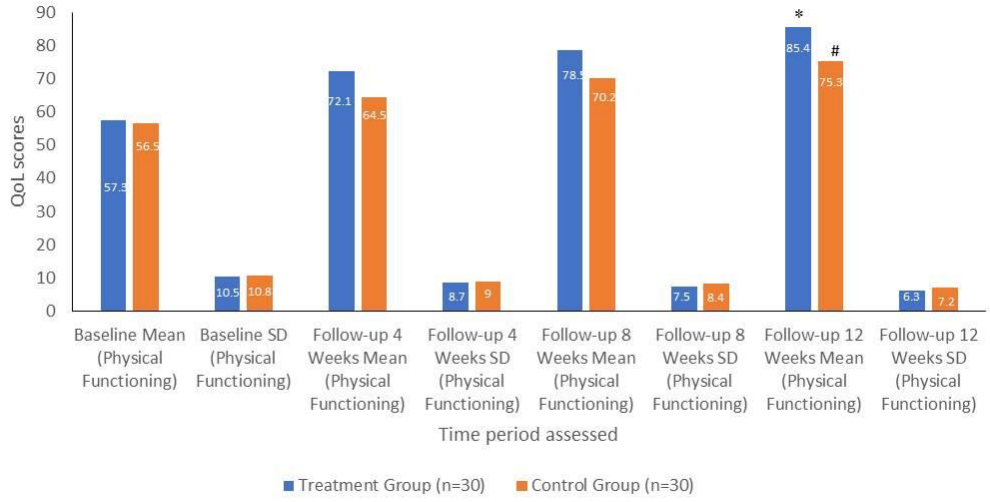

Figure 4. Quality of life-EORTC QLQ-C30 scores (physical functioning) assessed.

Note: Compared with baseline of treatment group $^{*}p < 0.05$. Compared with baseline of control group $^{\#}p < 0.05$.

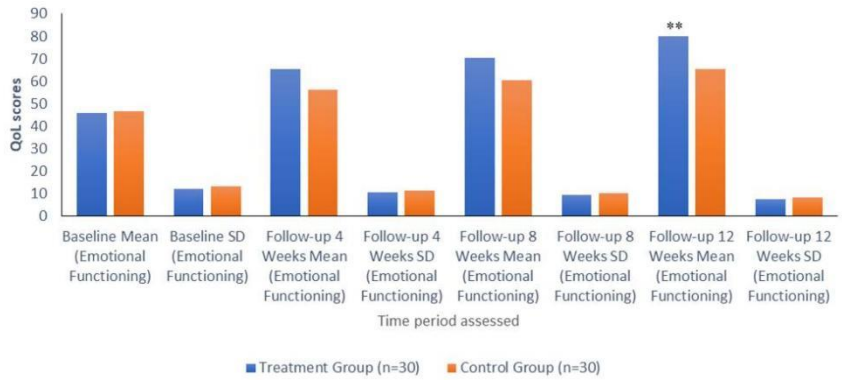

Figure 5. Quality of life-EORTC QLQ-C30 scores (emotional functioning).

Note: Compared with baseline of treatment group $^{**}p < 0.01$.

In addition, we also analyzed the systolic and diastolic blood pressure of two groups. At baseline, the mean systolic blood pressure for the treatment group was 142.3 mmHg (*SD* = 12.5, **Figure 6**), and for the control group it was 140.8 mmHg (*SD* = 13.2, **Figure 6**). After 12 weeks of treatment, the systolic blood pressure of the treatment group significantly decreased to 118.6 mmHg (*SD* = 8.9, *p* = 0.001, **Figure 6**), while the control group experienced a lesser decrease to 133.2 mmHg (*SD* = 11.3, *p* = 0.04, **Figure 6**). For diastolic pressure, the mean in the treatment group decreased from 89.1 mmHg (*SD* = 7.8) to 75.8 mmHg (*SD* = 6.1, *p* = 0.004), and that of the control group was minimally decreased from 88.5 mmHg (*SD* = 8.1) to 81.4 mmHg (*SD* = 6.8). These results showed that Wu's Long-Snake-Like Moxibustion was indeed successful in lowering systolic and diastolic blood pressure, a critical management area of hypertension among post-stroke cancer patients.

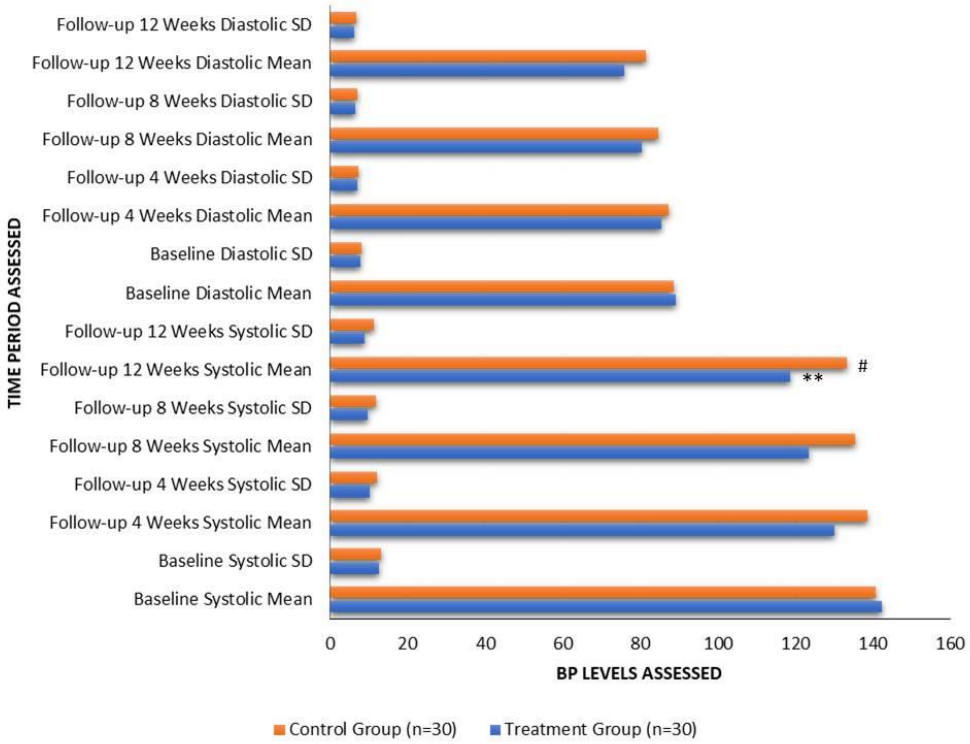

Figure 6. Blood pressure (hypertension)—systolic and diastolic blood pressure.

Note: Compared with baseline of treatment group $^{**}p < 0.01$. Compared with baseline of control group $^{\#}p < 0.05$.

Table 2 shows the paired *t*-test results of intra-group changes in the treatment group. All measures showed significant improvements, including psychological distress (HADS-A and GAD-7), sleep quality (PSQI), quality of life (physical and emotional functioning), and blood pressure (systolic and diastolic). For example, the treatment group showed a significant decrease in anxiety (HADS-A) with a mean difference of 9.1 ($p = 0.02$), and a significant decrease in systolic blood pressure with a mean difference of 23.7 mmHg ($p = 0.001$). These results proved the effectiveness of Wu's Long-Snake-Like Moxibustion in treating the physical and psychological problems of post-stroke cancer patients.

Table 2. Paired *t*-tests for within-group changes (treatment group).

Measure	Baseline Mean	Follow-up 12 Weeks Mean	Mean Difference	Standard Deviation of Difference	Paired *t*-test *p*-value
HADS-A	14.2	5.1	9.1	2	0.02
GAD-7	15	5.3	9.7	2.8	0.01
PSQI	8.7	3.2	5.5	1.6	< 0.0001
Physical Functioning	57.3	85.4	28.1	6.3	0.01
Emotional Functioning	45.8	80.1	34.3	7.3	0.002
Systolic BP	142.3	118.6	23.7	8.9	0.001
Diastolic BP	89.1	75.8	13.3	6.1	0.004

Table 3 reports the results of paired *t*-tests for intra-group changes in the control group. The anxiety (HADS-A) and blood pressure also improved in the control group, but to a lesser extent than in the treatment group. For example, the mean difference of HADS-A was 3.5 (p = 0.04), and the decrease in systolic blood pressure was 7.6 mmHg (p = 0.04). Therefore, the results showed that although standard care had improved in some indicators, the treatment group had gained more significantly from the intervention.

Table 3. Paired *t*-tests for within-group changes (control group).

Measure	Baseline Mean	Follow-up 12 Weeks Mean	Mean Difference	Standard Deviation of Difference	Paired *t*-test *p*-value
HADS-A	13.9	10.4	3.5	3	0.04
GAD-7	14.7	11.1	3.6	3.8	0.03
PSQI	8.3	6.7	1.6	1.8	0.05
Physical Functioning	56.5	75.3	18.8	7.2	0.04
Emotional Functioning	46.5	65.4	19.9	8.2	0.05
Systolic BP	140.8	133.2	7.6	11.3	0.04
Diastolic BP	88.5	81.4	7.1	6.8	0.03

Table 4 summarizes the results of independent *t*-tests between the treatment and control groups at the 12-week follow-up. There were significant differences between the two groups in anxiety (HADS-A), sleep quality (PSQI), and quality of life (physical and emotional functioning), with greater improvements in the treatment group. For example, the mean HADS-A score of the treatment group was 5.1, while the control group was 10.4 (p = 0.02). This showed that Wu's Long-Snake-Like Moxibustion had a stronger effect on alleviating psychological distress. Similarly, the physical functioning and emotional functioning of the treatment group were significantly better than those of the control group, with differences of 10.1 (p = 0.01) and 14.7 (p = 0.002), respectively.

Table 4. Independent *t*-tests for between-group differences (treatment vs. control) at 12 weeks.

Measure	Treatment Mean (12 Weeks)	Control Mean (12 Weeks)	Mean Difference	Independent *t*-test *p*-value
HADS-A	5.1	10.4	−5.3	0.02
GAD-7	5.3	11.1	−5.8	0.03
PSQI	3.2	6.7	−3.5	0.0001
Physical Functioning	85.4	75.3	10.1	0.01
Emotional Functioning	80.1	65.4	14.7	0.002
Systolic BP	118.6	133.2	−14.6	0.01
Diastolic BP	75.8	81.4	−5.6	0.04

4. Discussion

4.1. Significance and future implications of this study

The findings of this study indicate that Wu's Long-Snake-Like Moxibustion can

provide substantial therapeutic benefits for post-stroke cancer patients, addressing psychological and physiological challenges. The significant reduction in psychological distress (anxiety and depression) and improvement in sleep quality suggest that this therapy can be a valuable intervention for improving mental health. Additionally, the improvement in physical functioning and emotional stability demonstrates the potential of Wu's Long-Snake-Like Moxibustion in enhancing the overall quality of life for this complex patient population. The regulation of hypertension observed in the treatment group further supports the holistic approach of Wu's Long-Snake-Like Moxibustion, as managing blood pressure is crucial for reducing the risks associated with stroke and cancer comorbidities. Future studies should explore the long-term effects of this therapy and investigate its mechanisms of action in more detail, potentially incorporating it into standard clinical practice to improve the health outcomes of post-stroke cancer patients.

4.2. Microglial involvement in neuroinflammation and depression

The neuroinflammatory response in depression is predominantly mediated by glial cells, particularly microglia, which acts as the resident macrophages of the central nervous system (CNS) [21]. Microglia is derived from myeloid progenitor cells and plays a pivotal role in protecting neurons from damage caused by neurotoxic agents. They are also involved in a range of neurodegenerative diseases, including depression, Alzheimer's disease, and Parkinson's disease. Microglia provides essential neurotrophic support and contributes to maintaining neuronal health [22–24]. They account for about 5% to 10% of the brain's total cell population and can respond to inflammatory stimuli by producing pro-inflammatory cytokines and prostaglandins. Their activation of cell damage may contribute to the neuroinflammatory environment characteristic of depression [25].

4.3. Role of HMGB1 in neuroinflammation and depression

High-mobility group box 1 (HMGB1) is a pro-inflammatory molecule that functions as both a gene transcription regulator and a structural protein within the nucleus. Emerging research suggests that HMGB1 is involved in the pathogenesis of depression, particularly in response to cellular stress and inflammatory processes [26]. Under inflammation conditions, HMGB1 is released from the nucleus and transferred to the cytoplasm, where it binds to the TLR4 receptor. This binding triggers the TLR4/NF-κB signaling pathway, initiating an inflammatory cascade that leads to the development of depression-like symptoms [27]. Experimental models such as chronic unpredictable mild stress (CUMS) and lipopolysaccharide exposure demonstrate the activation of the HMGB1/TLR4/NF-κB pathway in depression [28–30]. These findings suggest that targeting this pathway can provide a therapeutic approach for managing depressive symptoms by regulating neuroinflammation.

4.4. HMGB1/TLR4/NF-κB pathway as a target for depression therapy

Research has increasingly focused on the HMGB1/TLR4/NF-κB signaling pathway as a key mechanism of neuroinflammatory response associated with depression. HMGB1 is a protein known for modifying DNA structure and plays an

integral part in the occurrence of inflammation [31–34]. It interacts with multiple receptors, of which TLR4 is particularly important in depression. When HMGB1 binds to TLR4, it activates the MyD88 protein, which activates the NF-κB signaling pathway. This activation exacerbates the inflammatory response, leading to depression-like behavior in experimental models [5,11]. HMGB1 is passively released in stress response and plays a central role in the inflammatory process, further enhancing its potential as a therapeutic target [30]. The application of Wu's Long-Snake-Like Moxibustion, a traditional therapeutic method, significantly reduced HMGB1 expression, suggesting that this treatment may mitigate depression by regulating the inflammatory response.

4.5. TLR4 signaling and depression

TLR4 is known to play a critical role in triggering the release of various cytokines, which communicate with the brain through molecular and cellular pathways [35]. This signaling may lead to inflammation within the central nervous system, which may exacerbate depression. Both acute and chronic stress have been shown to activate TLR4 signaling pathways in peripheral and central systems, leading to depression-like behaviors [35,36]. Studies have indicated that blocking the TLR4/MyD88 signaling pathway can alleviate depressive symptoms, suggesting that TLR4 is an important target for therapeutic interventions [37–39]. An increase in the expression of TLR4 and MyD88 proteins was observed in experimental models of depression, and the expression of these proteins was significantly reduced after treatment with Wu's Long-Snake-Like Moxibustion [40]. This suggests that Wu's Long-Snake-Like Moxibustion may regulate the inflammatory pathways involved in depression, providing a potential therapeutic option for managing depression-like behaviors by targeting TLR4 signaling in the central nervous system.

4.6. Limitations

This study has several limitations that should be taken into account when interpreting the findings. Although the sample size is sufficient, it is relatively small and limited to a specific patient population, which may not fully represent the broader group of post-stroke cancer patients. The cancer types included in this study were only lung cancer and breast cancer. Other cancer types, including hematologic cancers, should be included in the follow-up study, so that the research results can be extended to more types of cancer patients. In addition, the study's observational period was only 12 weeks, which may not capture the long-term effects of Wu's Long-Snake-Like Moxibustion. Further, although the study demonstrated significant improvements, the absence of biomarkers or a mechanistic analysis of how Wu's Long-Snake-Like Moxibustion affects the underlying physiological processes limits the generalizability of the results.

5. Conclusion

Wu's Long-Snake-Like Moxibustion has significantly improved the psychological distress, sleep quality, quality of life, and hypertension management of post-stroke cancer patients. These results suggested that this therapy could serve as an

effective complementary treatment, providing a comprehensive approach to managing the physical and emotional challenges faced by this patient population. Future studies with larger sample sizes and longer follow-up periods are recommended to confirm these findings and explore the underlying mechanisms of action.

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Informed consent statement: Written informed consent was obtained from all participants prior to enrollment. Patient and healthcare worker information was kept confidential during the study.

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