Prevalence and Influencing Factors of Upper Limb Musculoskeletal Disorders Associated with Paclitaxel in Surgically Treated Women with Breast Cancer: A Secondary Cross-Sectional Descriptive Study

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Abstract:

Background and Objective: Breast cancer is the most prevalent malignancy among women worldwide. Despite significant advances in surgical techniques, radiotherapy, and chemotherapy, complications such as paclitaxel-induced peripheral neuropathy continue to severely impact patients' quality of life. Paclitaxel disrupts microtubule dynamics and axonal transport, leading to nerve damage and functional impairments in the upper limbs. The combined effects of surgical interventions, radiotherapy, and paclitaxel treatment further increase the risk of developing musculoskeletal disorders. Therefore, this study aims to investigate the prevalence and contributing factors of upper limb musculoskeletal disorders associated with paclitaxel in women who have undergone surgical treatment for breast cancer.

Materials & Methods: This descriptive cross-sectional study was conducted at Tabriz University of Medical Sciences. The study sample consisted of women aged 18 years and older who had been diagnosed with breast cancer, undergone surgery, and were candidates for treatment with paclitaxel and radiotherapy. A convenience sampling method was employed based on a pre-calculated sample size, resulting in the inclusion of 100 patients. Demographic and clinical data were systematically collected, and musculoskeletal issues were evaluated through standardized physical examinations focusing on the shoulder, elbow, carpal tunnel syndrome, and tenosynovitis of the thumb. Patients were classified according to the affected—either the affected side or the healthy side—and the prevalence of musculoskeletal disorders on each side was assessed. Statistical analyses included the Mann-Whitney U test, Chi-square test, and t-tests for qualitative data assessment, with a significance level set at $p < 0.05$.

Results: The physical examination of the shoulder revealed significant findings, with the highest rates of negative outcomes observed in the Cross Over test (69%; 69 patients) and the Yergason test (66%; 66 patients). The Empty Can test indicated a positive response in 21% (21 patients) on the affected side, while 8% (8 patients) exhibited bilateral positive responses. Furthermore, the Neer Impingement test showed positive findings in 23% (23 patients) on the affected side and 12% (12 patients) bilaterally. The Hawkins-Kennedy test revealed positive results in 20% (20 patients) on the affected side and 9% (9 patients) bilaterally. The Compression test was positive in 25% (25 patients) on the affected side, with only 2% (2 patients) reporting bilateral positive findings on the Cross Over test, illustrating varied patterns of shoulder structural involvement among participants.

Conclusion: The findings of this study indicate that musculoskeletal disorders and shoulder pathologies in surgically treated women with breast cancer receiving paclitaxel predominantly occur on the affected side, with a notably high prevalence of subacromial impingement, while acromioclavicular joint involvement is minimal. These results highlight the significant interplay among surgical effects, drug-induced neuropathy, and radiotherapy in the development of these disorders, underscoring the need for targeted assessments and rehabilitation strategies.

Keywords: Breast Neoplasms, Paclitaxel, Cross-Sectional Studies

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Received: 14/09/2025

Accepted: 19/02/2026

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Background and Objective

Breast cancer remains the most prevalent malignancy among women worldwide and is a major contributor to cancer-related morbidity and mortality.[1] Despite significant advancements in surgical techniques, radiotherapy, and chemotherapy that have enhanced survival rates, these improvements have also led to various treatment-related complications.[2] Among the most serious of these are neurological complications caused by chemotherapy, which can profoundly reduce the quality of life of affected patients.[3]

Paclitaxel, a microtubule-stabilizing agent from the taxane family, is a fundamental component of breast cancer treatment and is commonly used in both adjuvant and neoadjuvant therapeutic regimens.[4] This agent functions by stabilizing microtubules and inhibiting proper cellular division, while simultaneously disrupting the axonal transport mechanisms of sensory and motor neurons.[5] Such disruption can result in chemotherapy-induced peripheral neuropathy (CIPN), a condition that often affects both the upper and lower extremities and presents with a variety of symptoms, including tingling, numbness, pain, and muscle weakness.[6]

Among women with breast cancer who have undergone mastectomy or lumpectomy, several factors—including surgical effects, nerve damage, restricted shoulder mobility, radiotherapy-induced soft tissue fibrosis and vascular necrosis, and neural fiber dysfunction caused by paclitaxel—can collectively increase the risk of developing upper extremity neurological complications.[7] These complications may arise not only during the acute treatment phase but also persist or emerge months or even years after treatment completion.[8]

The incidence of CIPN associated with paclitaxel varies significantly across different studies. This variability is influenced by multiple factors, including cumulative dosage, infusion frequency, patient age, the presence of comorbidities such as diabetes, and prior neurological conditions.[9] Prevalence rates of CIPN have been reported to range from 30% to 80%, with even higher incidence observed among patients receiving combination therapies that include carboplatin or doxorubicin.[10]

At the pathophysiological level, paclitaxel disrupts the synthesis of essential proteins required for neuronal survival, alters axonal transport, and initiates inflammatory responses mediated by cytokines.[11] Investigations in animal models have also suggested that paclitaxel may reduce the density of small nerve fibers, cause alterations in myelination, and increased the sensitivity of pain receptors.[12]

From a clinical perspective, upper extremity neurological complications resulting from paclitaxel can severely impair daily functioning, hinder occupational and social activities, and increase dependence on caregivers.[13] This presents a significant challenge for cancer survivors striving to resume their pre-treatment lifestyles.[14]

The severity and duration of neurological complications associated with paclitaxel are influenced by various factors, including gender, advanced age, elevated body mass index, concurrent use of neurotoxic medications, and a history of peripheral nerve diseases.[15] Additionally, metabolic disorders such as vitamin B12 deficiency and thyroid dysfunction may exacerbate these complications.[16]

From a preventive healthcare perspective, identifying patients at risk before initiating paclitaxel treatment is essential. This can be achieved through careful dosage adjustments, regular monitoring of neurological symptoms, and the implementation of proactive intervention strategies, including physical therapy, antioxidant supplementation, and medication management, to reduce the incidence or severity of side effects.[17]

In light of improved survival rates among women diagnosed with breast cancer, contemporary research has increasingly focused on enhancing patients' quality of life after treatment.[18] A thorough examination of the prevalence and contributing factors of upper extremity neurological complications induced by paclitaxel could provide valuable insights for clinical decision-making, the development of supportive care protocols, and patient education. Consequently, the present study aims to evaluate the prevalence of upper extremity neurological issues associated with paclitaxel treatment in women who have undergone surgical interventions for breast cancer.

Materials and Methods

Study Design: This descriptive cross-sectional study was conducted at Tabriz University of Medical Sciences and involved women diagnosed with breast cancer who were candidates for chemotherapy following surgical intervention. Participants were selected according to specific inclusion and exclusion criteria established for the study.

Eligibility Criteria

The study included women aged 18 years and older who had been diagnosed with breast cancer, underwent surgical intervention, and were scheduled to receive paclitaxel chemotherapy and breast radiotherapy. Inclusion criteria required participants to complete a minimum of six sessions of radiotherapy and provide written informed consent. Exclusion criteria comprised individuals with diabetes, cardiovascular diseases, thyroid disorders, lymphedema, a history of musculoskeletal disorders or cervical disc problems, metastatic disease, treatment-related cachexia, and those who had previously undergone surgeries involving the shoulder, elbow, or wrist joints. These criteria were established to minimize confounding variables and enable a focused evaluation of the neurotoxic effects of paclitaxel on the upper limbs.

Sampling

To determine an appropriate sample size, a sample size estimation formula was used for studies assessing proportions within a population. A prevalence rate of 30% was established based on findings reported by Shamley et al. With a type I error set at 0.05, a statistical power of 80%, and a study duration of 12 months, a total of 100 participants were recruited using a convenience sampling method.

Methods

Comprehensive demographic data were collected from participants, including age, weight, height, side of surgery, the extremity affected by musculoskeletal problems, treatment received, history of chemotherapy (including the number of sessions completed), number of radiotherapy sessions, and the status of diabetes, hypertension, and smoking. Standardized physical examinations were conducted to diagnose musculoskeletal issues, with a positive result in at least one test per diagnostic area indicating the presence of a problem. Diagnostic evaluations for shoulder issues included the Empty Can test, Neer's test, Hawkins-Kennedy test, Yergason's test, Speed's test, and Cross-Body test. For tennis elbow, assessments included the Resisted Tennis Elbow test, Cozen's test, and Passive Tennis Elbow test. Carpal tunnel syndrome evaluations comprised the Phalen's test, Reverse Phalen's test, Tinel's sign, and Pronator Teres test. To evaluate tenosynovitis of the thumb (de Quervain's), the Finkelstein test was used alongside isometric resistance maneuvers. All results for each participant were systematically recorded on a dedicated data collection form, which was subsequently subjected to comprehensive statistical analysis.

Statistical Analyses

The collected data were entered into SPSS statistical software for analysis. Frequencies, percentages, means, and standard deviations were calculated for quantitative data. For qualitative data, the Mann-Whitney U test, Chi-square test, and t-test were used to assess differences and associations. A p-value of less than 0.05 was considered statistically significant in all analyses.

Ethical Considerations

This study was conducted in accordance with established ethical standards and received approval from the Regional Ethics Committee of Tabriz University of Medical

Sciences (IR.TBZMED.REC.1400.1157) and the necessary permissions from the administrative authorities of Imam Reza and Shahid Madani Hospitals. Prior to the commencement of the study, all participants were thoroughly informed about the research objectives and provided written informed consent, confirming their voluntary participation. Additionally, participants were assured of their right to withdraw from the study at any time without experiencing any repercussions or adverse consequences.

Table 1- Summary of basic information of study participants

Variable		Value
Age	Mean±standard deviation	55.85±12.31
	Under 65 years	79 people–79%
	Above 65 years	21 people-21%
Height		168.49±24.59
Weight		77.40±3.55
BMI	Mean±standard deviation	24.01±3.14
	Below normal range	25 people-25%
	Normal	41 people-41%
	Above normal range	44 people-44%
Smoking	Yes	9 people-9%
	No	91 people-91%
History of blood pressure	Yes	41 people-41%
	No	59 people-59%
History of diabetes mellitus	Yes	24 people-24%
	No	76 people-76%

Findings

The mean age of participants in this study was 55.85 ± 12.31 years. Among the sample, 79 individuals (79%) were under 65 years of age, while 21 individuals (21%) were 65 years or older. The average height of the participants was 168.49 ± 24.59 cm, and the mean weight was 77.40 ± 3.55 kg. The mean body mass index (BMI) was 24.01 ± 3.14, with 25 individuals (25%) classified as underweight, 41 individuals (41%) within the normal range, and 34 individuals (34%) categorized as overweight or obese. A history of smoking was reported by 9 individuals (9%), whereas 91 individuals (91%) had never smoked. Hypertension was present in 41 individuals (41%), while 59 individuals (59%) were free of this condition. Additionally, 24 individuals (24%) reported a history of diabetes mellitus, and 76 individuals (76%) were confirmed to be without diabetes (Table 1).

Further examination of disease-related characteristics indicated that 41 participants had right breast involvement. The mean number of chemotherapy sessions received was 2.85 ± 9.24, and participants underwent an average of 24.59 ± 5.41 radiotherapy sessions (Table 2).

Table 2- Review of disease-related information in study participants

Variable		Value
Side of conflict	Right	41 people-41%
	Left	59 people-59%
Chemotherapy sessions	Mean±SD	9.2 ± 2.85
	Under 6 sessions	21 people-21%
	6 to 12 sessions	59 people-59%
	More than 12 sessions	20 people-20%
Radiotherapy sessions	Mean±SD	24.5 ± 5.41
	Under 10 sessions	11 people-11%
	10 to 20 sessions	69 people-69%
	More than 20 sessions	20 people-20%

Participants were categorized according to the side affected by breast cancer, enabling a comparative analysis of the incidence of musculoskeletal disorders between the affected and unaffected sides. Diagnostic assessments of the shoulder revealed that the Neer impingement test yielded the highest frequency of positive results among women undergoing radiotherapy, while the Cross-Body test exhibited the lowest frequency of related shoulder pathologies (Table 3).

Table 3- Results of shoulder physical tests in patients participating in the study

Relevant test	Negative	Positive on affected side	Positive on unaffected side	Positive on both sides
Empty Can	59 people-59%	21 people-21%	12 people-12%	8 people-8%
Neerimpingment	55 people-55%	23 people-23%	10 people-10%	12 people-12%
Hawkins Kennedy Impingement	61 people-61%	20 people-20%	10 people-10%	9 people-9%
Yergason's Test	66 people-66%	20 people-20%	10 people-10%	4 people-4%
Compression Test	62 people-62%	25 people-25%	8 people-8%	5 people-5%
Cross Over	69 people-69%	20 people-69%	9 people-69%	2 people-2%

Discussion

The findings of this study indicate a higher incidence of musculoskeletal disorders and functional limitations of the shoulder on the affected side in women who have undergone surgical treatment for breast cancer while receiving paclitaxel therapy. This observation may be attributed to various pathophysiological mechanisms associated with surgical interventions, systemic treatments, and radiotherapy. Specifically, mastectomy or lumpectomy in combination with the excision of axillary lymph nodes leads to direct damage to soft tissues and alterations in the biomechanics of the shoulder girdle, which contribute to the formation of adhesions around muscles and tendons. Consequently, these factors have a more pronounced impact on the affected side.[6]

Paclitaxel, a chemotherapeutic agent known for its cytotoxic effects on tumor cells, also induces dose-dependent peripheral neuropathy, a condition influenced by the duration of exposure to the medication.[7] This neuropathy affects both sensory and motor nerve fibers in the upper limb, resulting in reduced neural control over shoulder musculature and subsequently causing pain and weakness.[8] In patients who have also undergone radiotherapy, the combined effects of inflammation and tissue fibrosis around the shoulder joint further exacerbate this neuromuscular weakness, increasing the likelihood of positive clinical findings indicative of shoulder pathology.[9,10]

Our findings reveal that the Neer impingement test yielded the highest rate of positive results, consistent with the expected pathologies in patients receiving treatment for breast cancer.[11] Specifically, a reduction in the subacromial space, combined with increased stiffness in the tissues surrounding the supraspinatus tendon—outcomes influenced by surgical scarring and inflammatory changes resulting from radiotherapy—are recognized contributors to subacromial impingement.[12] Furthermore, repetitive stress on the tendon and surrounding musculature, caused by altered shoulder biomechanics, intensifies the stimulation of pain receptors and contributes to limitations in range of motion.[13]

Conversely, the Cross-Body test exhibited the lowest frequency of positive results.[14] This test is primarily used to evaluate damage to the acromioclavicular joint;[15] however, the findings in our patient population were less favorable, likely because the focus was predominantly on subacromial tissues and rotator cuff muscles rather than on limitations specific to the acromioclavicular joint itself. Additionally, it is noteworthy that common surgical interventions for breast cancer generally do not involve direct manipulation of this joint. when associated damage occurs, it is more frequently attributed to trauma or degenerative changes related to aging.[16]

Another significant aspect to consider is the observed disparity in test outcomes between the affected and healthy sides. Although nerve damage caused by paclitaxel occurs even on the healthy side, the mechanical stresses and structural changes associated with surgery and radiotherapy are primarily limited to the affected side, resulting in milder symptoms on the contralateral side.[17] Nonetheless, the development of disorders on the healthy side highlights the role of systemic factors, such as drug-induced neuropathy, which can impact both upper limbs, albeit with greater severity on the affected side.[18]

Moreover, the positive results from tests conducted on both sides—including the Empty Can and Hawkins–Kennedy tests—indicate a combined effect of systemic factors and compensatory alterations in shoulder movement. The reduced activity on the affected side throughout the course of treatment leads to increased reliance on the healthy side, which can ultimately result in functional shoulder disorders, a condition frequently referred to as "overuse Injury."[19] This pattern suggests that the implications of paclitaxel extend beyond neuropathic effects, potentially contributing to the development of secondary injuries through alterations in muscle utilization patterns.[11]

From a clinical perspective, the interpretation of the findings from this study has significant implications for rehabilitation programs. By identifying the most vulnerable areas, such as the subacromial region, clinicians can make informed decisions regarding appropriate stretching and strengthening exercises, as well as manual therapy techniques.[20] Furthermore, routine evaluation of shoulder clinical tests in patients undergoing treatment with paclitaxel and radiotherapy enables healthcare providers to detect injuries at early stages, thereby facilitating timely interventions to prevent their progression.[15]

The onset of these disorders is influenced by a complex interplay of factors, including paclitaxel-induced neuropathy, the structural effects of surgical interventions, and the inflammatory consequences of radiotherapy. This multifactorial mechanism initiates a cascade of changes, beginning with nerve damage, which leads to impaired muscle performance and altered biomechanics, ultimately manifesting as clinically recognizable symptoms during physical assessments. Consequently, treatment strategies that focus exclusively on a single factor are often inadequate.[13] A comprehensive approach that integrates pain management, movement re-education, and activity patterns modifications is essential for effective rehabilitation.[11]

Conclusion

The findings of this study reveal that musculoskeletal disorders and shoulder pathologies predominantly occur on the affected side in women who have undergone surgical treatment for breast cancer and are receiving paclitaxel. The most prevalent condition identified was subacromial impingement, while damage to the acromioclavicular joint was the least common. These results highlight the critical role of the combined effects of surgical interventions, drug-induced neuropathy, and radiotherapy in the development of these disorders. Therefore, targeted assessment and rehabilitation strategies are essential to optimize patient care.

Acknowledgments

This summary presents supplementary findings from a broader study that is currently under review in a comprehensive format suitable for ISI publication. The authors sincerely thank Mr. Alireza Naseri and Dr. Sina Ebrat Khah, who, at their request, have chosen to remain unnamed in this supplementary article.

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