



Investigating the Factors Affecting the Severity of Neuropathic Pain Before and After the Coronavirus Infection in Patients Having Breast Cancer Surgery

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Abstract

Objectives: Approximately one-third of women having breast surgery experience neuropathic pain although no study has so far identified its risk factors. It seems that the coronavirus infection increases the likelihood of neuropathic pain through influencing the neuropsychological system. Therefore, the current study aimed to investigate factors affecting the severity of neuropathic pain before and after coronavirus disease 19 (COVID-19) in patients who had breast cancer surgery.

Materials and Methods: The current descriptive-analytical study was conducted six months before June 4, 2020. In total, 40 women having breast surgery participated in this study. Postoperative neuropathic pain and its influencing factors were evaluated using demographic tools, Spielberger anxiety, and a 36-item short-form health survey for measuring the quality of life (QoL). Finally, data were analyzed by multivariate regression.

Results: Neuropathic pain significantly increased during the COVID-19 pandemic. Mastectomy ($P=0.009$), removal of lymph nodes ($P=0.011$), number of radiotherapy sessions ($P=0.003$), history of chemotherapy ($P=0.009$), disease stage ($P=0.015$), hidden anxiety ($P=0.005$), and explicit anxiety ($P=0.001$), and all domains of QoL ($P<0.05$) significantly predicted neuropathic pain.

Conclusions: In general, adverse effects of coronavirus pandemic reduced the QoL while increasing anxiety (hidden and explicit), thus leading to an increase in the severity of postoperative neuropathic pain.

Keywords: Neuropathic Pain, COVID-19, Breast Surgery, Anxiety

Introduction

Breast cancer is one of the most prevalent cancers in women and its incidence has substantially increased in recent decades (1,2). Surgery is the most common procedure for removing the cancer tissue. A part of the tissue or the entire tissue is removed during the surgery (3, 4). Chemotherapy may be administered before or after the diagnosis of breast cancer, and radiotherapy usually starts after breast surgery. However, it has several side effects including physical, psychological, and psychological complications, which may cause problems for the patient at different stages of treatment (5-8).

Neuropathic pain is one of the main complications. The International Association for the Study of Pain (IASP) defined neuropathic pain as an increase in the pain following direct injury or a disease that affects the neural system (the central, peripheral, or both) (9). This complication may have various causes, including when there is pressure on or infiltration of the central or peripheral nervous system, history of diseases such as diabetic neuropathy, surgery, and damage to the nervous system of the surgical area, or following radiotherapy and chemotherapy and other psychological factors such as

stress and anxiety (9,10).

Neuropathic pain has a prevalence rate of 13%-35% and can adversely affect the course of treatment in many patients. However, the shares of its risk factors are still unknown since no study has so far focused on its mechanism (11). A study investigating factors affecting the severity of postoperative pain reported the importance of psychological factors including hidden and explicit stress and anxiety, along with physical factors associated with the surgery. However, the involved factors and their effects are yet unknown (12).

Given that the COVID-19 pandemic has increased the psychological tensions of those who are prone to coronavirus infection (13), especially women who had a mastectomy, the current study sought to investigate the prevalence of neuropathic pain before and during the COVID-19 pandemic in women who had a mastectomy.

Materials and Methods

Study Design

This descriptive-analytical study was conducted on women with mastectomy referring to the oncology clinics of Tabriz University of Medical Sciences (TUMS) three

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Key Messages

- ▶ The prevalence of neuropathic pain in breast cancer is reported to be nearly one-third.
- ▶ Neuropathic pain is directly related to physical and psychological factors.
- ▶ Critical conditions in the corona pandemic increased the severity of neuropathic pain after breast surgery.

months before the COVID-19 pandemic and during the first trimester of the pandemic outbreak in Iran (March 5, 2020 to June 4, 2020). The sample size was estimated based on (14) using the following formula:

$$n = \left(\frac{z_{1-\frac{\alpha}{2}} + z_{1-\beta}}{0.5 \ln\left(\frac{1+r}{1-r}\right)} \right)^2 + 3$$

The statistical power and the confidence coefficient were considered as 80% and 95%, and the maximum correlation between neuropathic pain factors in the preliminary study was equal to -0.43 (35 subjects).

By considering a drop-out rate of 15%, the total sample size was estimated as 40. Participants were selected using the convenience sampling method among those referring to Shahid Madani and Ghazi Tabatabai hospitals to follow up their treatments. The inclusion criteria were being diagnosed with breast cancer (approved by a thorax surgeon and a pathologist), being aged at least 18 years, giving informed consent for participation, and obtaining a pain score above six for at least three months. On the other hand, the exclusion criteria included having a history of any type of cancer and coronavirus and systemic infections while no proper awareness to participate in the study.

Data Collection Tools

A three-part questionnaire was used to collect information. The first part that was about the demographic profile included data on age, level of education, body mass index (BMI), type of surgery (i.e., lumpectomy, mastectomy, or removal of lymph nodes), number of radiotherapy sessions, history of chemotherapy, and stage of the disease. The second part was the visual analogues scale (VAS) checklist (15). The VAS is designed to measure pain. This checklist is for the subjective measuring of the severity of the pain. The VAS is typically presented as a 10 cm line, in which 0 and 10 indicate “no pain” and “severe pain”, respectively. The State-Trait Anxiety Inventory (STAI, both hidden and Explicit) was used to assess the level of anxiety (16). The scores of each domain of the STAI range from 20 to 80 and a higher score represents higher anxiety. The SF-36 quality of life (QoL) tool was used to assess the QoL (17). This tool measures eight dimensions of physical and mental health, and its final score varies from 0 to 100, and a higher score demonstrates higher QoL. The final score

of each dimension of the questionnaire was multiplied by 100 to facilitate result evaluations.

Materials and Methods

In the first stage, all patients with breast cancer diagnoses referring to the oncology clinics of Shahid Madani and Ghalati Tabatabai hospitals (affiliated to TUMS) were identified and entered into the study, and they filled the questionnaire. In the second stage, among those who filled the questionnaire, those meeting the inclusion criteria entered the study. The pain questionnaire was filled once a month by the patient or a first-degree relative of the patient. Neuropathic pain is defined as having pain in the chest, chest wall, axillary or the middle arm, the affected area, the area of breast surgery, or the hands/feet (secondary to peripheral neuropathy) for at least 24 hours caused by chemotherapy. The IASP scoring system was used to categorize pain for the diagnosis of neuropathic pain. In this system, neuropathic pain is defined as having pain for at least three months based on the VAS checklist. Pain scores less than 3, 3-6, and higher than 6 are categorized as mild; moderate, and severe neuropathic pain, respectively (14). Considering that the study began before the coronavirus pandemic outbreak, all information was collected through face-to-face conversations in the clinics before the pandemic.

Statistical Analysis

After obtaining informed consent, patients completed the relevant questionnaires. The questionnaires were completed once a month (six times in total) for patients who were referred to the mentioned hospitals for chemotherapy for six months. The obtained data were analyzed using SPSS software (version 20) and quantitative data were presented as the mean \pm standard deviation. Eventually, a multivariate regression test was used to investigate the association between the variables, and $P < 0.05$ was considered statistically significant.

Results

The mean age and the mean of the BMI of the participants were 55.25 ± 11.42 years and 26.15 ± 03.18 , respectively. In general, 32 (80%) out of 40 participants were over 50 years, and most participants (31 or 77.5%) had more than 20 sessions of radiotherapy. Demographic information is presented in Table 1.

The mean \pm SD of participants' pain intensity in the first and second trimesters were 06.75 ± 1.15 and 07.50 ± 1.20 , respectively. Moreover, the mean \pm SD of the severity of anxiety in the first and second trimesters were 118.85 ± 12.40 and 145.15 ± 15.10 , respectively. For QoL, the mean \pm SD in the first and second trimesters were 59.45 ± 5.65 and 39.20 ± 4.25 , respectively. The comparison of the severity of pain, anxiety (both hidden and explicit), and dimensions of QoL indicated that the mean \pm SD

Table 1. Individual-social Characteristics of Study Participants

Variable	Mean \pm SD/N (%)
Age (y)	55.25 \pm 11.42
>50	32 (80%)
<50	8 (10%)
BMI	26.15 \pm 03.18
Lumpectomy	15 (18.75%)
Mastectomy	45 (56.25%)
Removal of lymph nodes	20 (25%)
Number of radiotherapy sessions	
>10	15 (18.75%)
10-20	49 (61.25%)
<20	16 (20%)
History of chemotherapy	
Yes	55 (68.75%)
No	25 (31.25%)
Stage	
0	6 (07.50%)
I	13 (15%)
II	16 (20%)
III	20 (25%)

scores of all dimensions significantly decreased during the second trimester (Table 2). On the other hand, investigating the severity of neuropathic pain, anxiety, and QoL demonstrated a gradual increase in the scores (Figure 1).

According to the regression results, mastectomy ($P=0.009$), removal of lymph nodes ($P=0.011$), number of radiotherapy sessions ($P=0.003$), history of chemotherapy ($P=0.009$), disease stage ($P=0.015$), hidden anxiety ($P=0.005$), and explicit anxiety ($P=0.001$), and all domains of the QoL ($P>0.05$) significantly predicted neuropathic pain. Table 3 provides the results of multivariate regression analysis for neuropathic pain.

Discussion

The current study presented a comprehensive description of the effects of factors affecting neuropathic pain in

patients who had breast cancer surgery. Cancers, including breast cancer, weaken the immune system following medications such as chemotherapy and radiotherapy, and weak immune systems can predispose people to a variety of diseases. Therefore, in the coronavirus pandemic, people with cancer have been identified as having a high risk of developing the disease, and these people should be highly careful about methods of preventing the disease. Previous research has shown that cancer increases the risk of developing coronavirus-like viruses, and these people are more susceptible to severe acute respiratory syndrome and the Middle East respiratory syndrome compared to other individuals (18). According to the results, neuropathic pain in women having breast cancer surgery was higher during the coronavirus pandemic compared to before the pandemic. In addition, it was found that the mastectomy, removal of lymph nodes, number of radiotherapy sessions, history of chemotherapy, stage of the disease, hidden and explicit anxiety, and all domains of the QoL can significantly predict neuropathic pain. In this regard, the results of the current study are consistent with those of other similar studies on factors affecting neuropathic pain after breast surgery (19,20).

Breast cancer surgery has many complications such as nausea and vomiting (21), edema, lymphedema (2), and severe pain. Pains and disabilities caused by surgery can lead to neuropathic pain. In the current study, several factors were identified, which can predict postoperative neuropathic pain. The extent of the surgery and removal of the lymph nodes, which require large incisions, can cause damage to the nervous system of the surgical area. Complementary treatments such as radiotherapy and chemotherapy can exacerbate the pain. It seems that the radiotherapy of breast cancer increases the pain, which can cause neuropathic pain due to the radiation to the breast tissue and the area close to the back.

Based on the results, anxiety (hidden or explicit) can predict postoperative neuropathic pain, which is consistent with the results of other similar studies (22-24). Based on the literature, high levels of anxiety can

Table 2. Comparison of Pain Intensity, Anxiety (Hidden and Explicit), and Dimensions of the Quality of Life

Variable	Before the Coronavirus Pandemic	During the Coronavirus Pandemic	P Value ^a
Neuropathic pain	06.75 \pm 1.15	07.50 \pm 1.20	0.012
State anxiety	58.15 \pm 6.15	79.45 \pm 10.35	0.001
Trait anxiety	55.40 \pm 6.80	85.80 \pm 10.45	0.003
Physical performance	59.15 \pm 5.35	69.40 \pm 6.15	0.036
Social functioning	42.40 \pm 5.20	66.15 \pm 6.30	0.012
Emotional role play	52.45 \pm 5.75	70.20 \pm 6.75	0.001
Physical role play	61.30 \pm 6.10	69.15 \pm 6.45	0.009
Mental health	69.10 \pm 6.70	52.50 \pm 5.30	0.011
Vitality	49.20 \pm 4.15	75.10 \pm 4.80	0.009
Pain	59.70 \pm 5.15	70.10 \pm 6.45	0.007
General health	40.35 \pm 5.60	63.25 \pm 6.20	0.008

Note. SD: Standard deviation. Data were expressed as mean \pm SD.

^a T test.

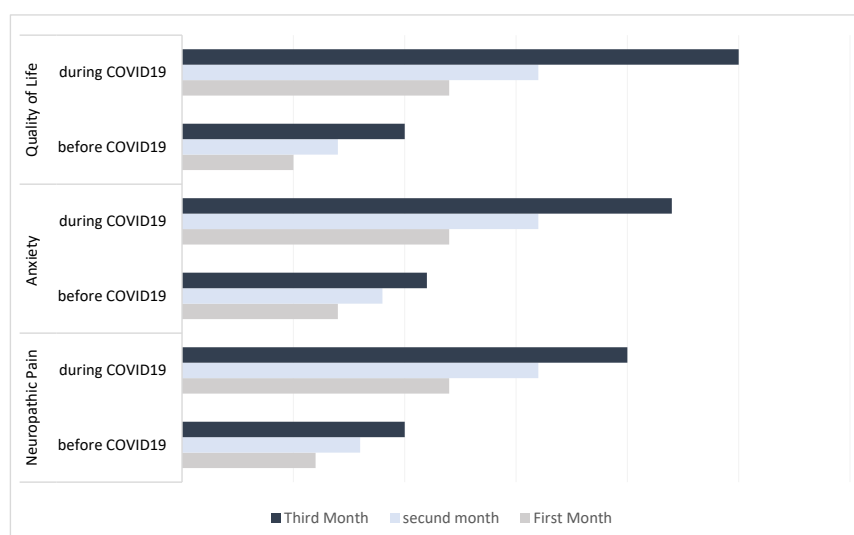


Figure 1. Neuropathic Pain, Quality of Life, and Anxiety of Participants Separated by Month. Note. COVID-19, coronavirus disease 19.

explain 35% of the pain associated with breast cancer surgery. In other words, high levels of anxiety are directly associated with neuropathic pain. It is believed that the increased level of anxiety leads to mechanisms in the body that interfere with the mechanism of pain and exacerbate the severity of pain. According to the results, high levels of stress during the COVID-19 pandemic significantly increased the severity of neuropathic pain.

Finally, the QoL and its dimensions could predict neuropathic pain in women who had breast surgery. Based on the results, the COVID-19 pandemic decreased the QoL of participants, and low QoL was found to be a predictor of neuropathic pain after breast surgery. In this regard, no study was found to report the same results. However, it seems that lower QoL, which consists of both physical and psychological dimensions, is associated with lower physical and mental capacity and/or weakness in coping abilities against factors such as pain, and the COVID-19 pandemic has exacerbated this issue.

Conclusions

The adverse effects of the coronavirus pandemic reduced the QoL while increasing the anxiety (hidden and explicit), thus leading to an increase in the severity of postoperative neuropathic pain.

Limitations of the Study

The current study was limited with the short study period, lack of awareness about the progression or regression of the degree of participants' disease, and loss of treatment plan that may lead to the worsening of the disease.

Suggestions for Future Studies

The authors recommend further studies on factors that cause neuropathic pain. Additionally, in the era of the COVID-19 pandemic, psychological measures are

necessary for reducing the mental problems of patients, which have negatively affected the patient's condition.

Authors' Contribution

SC: Study design and examination of patients; LG and HMA: Data collection and examination of patients; REZ: Examination of patients and article writing.

Conflict of Interests

Authors declare that they have no conflict of interests.

Ethical Issues

The current study was approved by the Ethics Committee of Tabriz University of Medical Sciences (Ethical Code: IR.TBZMED.REC.1397.598). Further, the authorities of Shahid Madani and Ghazi Tabatabai Hospitals were informed about all steps of the research. First, the objectives of the study were explained to potential patients. Then written consent was taken in case of their agreement for participation, and they were informed that participation is voluntary and can leave the research at any stage. Precaution measures were also made to prevent COVID-19 transmission.

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