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Prevalence and Risk Factors for Physical Impairments in Chinese Post-Cancer Treated Breast Cancer Survivors: A 4 Years' Cross-Sectional Study at a Single Center

*Chen D[1], Li L[1], Zhao YH[1], Jiang LY[1] and Jia J[1,2]**

[1]Department of Rehabilitation Medicine, Shanghai Jing'an District Central Hospital, China

[2]Department of Rehabilitation Medicine, Huashan Hospital Fudan University, China

Abstract

Objective: To examine the incidence, severity and risk factors of physical dysfunction in breast cancer survivors in China.

Methods: We collected the information on demographics and breast cancer treatments of breast cancer patients treated in the department of rehabilitation medicine of Jing'an District Central Hospital of Shanghai from January 2017 to December 2020.

Results: A total of 138 subjects were included in the study. The incidence of lymphedema (65.9%) was significantly higher than that of pain (31.2%), shoulder ROM restriction (20.3%), Grip strength restriction (21.7%) and paresthesia (11.6%). Although the differences were not statistically significant, the incidences of almost all of these impairments were higher in the first 28 months after breast cancer diagnosis than in other time periods. Cancer type and radiotherapy may be risk factors for the occurrence of lymphedema (respectively OR=6.18, 95% CI 1.85-20.72, p=0.003; OR=0.28, 95% CI 0.13-0.61, p=0.001). Radiation therapy and delayed rehabilitation may also increase the severity of lymphedema (respectively p=0.003; OR=0.28, 95% CI 0.13-0.61, p=0.010). The occurrence of pain, shoulder ROM restriction, grip strength restriction and paresthesia may be related to brachial plexus injury after breast cancer treatment.

Conclusion: The lack of professional medical resources for breast cancer rehabilitation and the incomplete referral system result in the delayed recovery of impairments that may occur in Chinese breast cancer survivors. This also prompts us to further investigate the actual rehabilitation needs of survivors and the specific barriers to rehabilitation in the following research.

Keywords: Breast cancer survivors; Lymphedema; Pain; Peripheral neuropathy; Rehabilitation

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Correspondence:
Jie Jia, Department of Rehabilitation Medicine, Shanghai Jing'an District Centre Hospital, No. 259 Xikang Road, Jing'an District, Shanghai, China, Tel: +86-021-61578411; E-mail: drjiajie@163.com

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Introduction

According to global Cancer Statistics 2020 [1], the incidence of breast cancer has surpassed lung cancer to become the most common malignant tumor worldwide. The incidence of breast cancer in Chinese women was 19.2% and showed an upward trend in the 2018 survey [2]. Moreover, the population of China has exceeded 1.4 billion, and the incidence of breast cancer shows a younger trend in the affected population [3]. Therefore, during clinical follow-up, which is the early detection of recurrence or metastasis, a higher attention should be paid to the function, quality of life and Return to Work (RTW) of breast cancer survivors [4]. Initially, breast cancer patients were treated with the classic radical mastectomy, first described by Halsted in 1894, involving the removal of the breast, pectoral muscles, and axillary lymph nodes [5]. The researchers noted that this surgery may be followed by obvious and frequent arm problems, such as lymphedema, reduced Range of Motion (ROM) of the shoulder, pain, numbness and muscle weakness [6]. With the rapid development of therapeutic concepts, in the second half of the 20th century, an innovative surgery was described by Patsy [7] and Madden [8] respectively, it aimed to preserve the main or both pectoral muscles, known as modified radical mastectomy, and causing less harm to the patients. Chemotherapy, radiation, and sentinel lymph node biopsies may also be used in time to avoid further tissue and lymph node removal. It provides a more accurate and less harmful treatment model for the clinical treatment of breast cancer, but the long-term sequelae still exist. Then the researchers realized that the determinants of sequelae are complex and may depend on the type of initial surgery, the number of lymph nodes removed, whether the contralateral breast was also removed (contralateral

prophylactic mastectomy), the type of reconstruction and adjuvant therapy.

Surgery can still trigger other physical changes. Mastectomy alters muscle distribution and biomechanics in the upper quadrant of the trunk, leading to a series of changes around the scapula that are likely to cause shoulder impingement and rotator cuff disease [4,9-14], which can further lead to shoulder pain [15], reduced range of motion, and muscle strength [16]. Sentinel Lymph Node Biopsy (SLNB) was also usually performed during breast surgery, and Axillary Lymph Node Dissection (ALNB) may be required if the sentinel biopsy is positive or if the patient has more advanced cancer. This axillary surgery not only increases the risk of arm damage, lymphedema, and chronic pain syndrome [17], but may also damage the intercostal brachial nerve and other brachial plexus nerves, causing abnormal sensation [18]. Abnormal sensations may occur in the chest wall, armpit, upper arm, and sometimes in the upper back and around the affected breast [19,20]. Radiation may also aggravate this injury [18]. In addition, adjuvant treatments, such as radiation, can also cause fibrosis and negatively affect the microvascular system [21], while the dose or volume of radiation can affect the outcome of shoulder function, including pain, stiffness [22], and mobility.

The incidence and presentation of above-mentioned sequelae have been reported, but the incidence and description vary somewhat due to assessment criteria and study design. In a 2018 cross-sectional study, Hamood et al. [19] reported that 84% of breast cancer survivors who were members of the "Leumit" Medical Fund in Israel had chronic pain and 63% had paresthesia [19]. In a prospective observational study in the United States, 10% breast cancer survivors had decreased ROM, 49% had pain, and 47.1% had numbness at 12+ months after surgery [23]. A 10-year cohort study in the United States reported that chronic lymphedema occurred in 5/108 (4.6%) and 40/115 (34.8%) of the SLND and ALND groups, respectively [24]. In a cohort study in Spain, Monleon et al. [25] found that compared with SLNB surgery, the strength of internal rotator muscle after ALND in breast cancer decreased significantly in the first month, and still did not recover after 1 year of follow-up, with an average difference of 2.26 kg [25]. A one-year prospective observational study in Korea found that shoulder strength and ROM returned to baseline one year after latissimus dorsi flap surgery. However, the physical aspects of functional disability and deterioration of quality of life remained [26]. In a 5-year longitudinal study, Boquiren et al. [27], Canada, found that restricted ROM and pain, except for lymphedema, peaked one year after surgery and then declined significantly after 5 years [27]. However, there are few studies on the occurrence and development of postoperative sequelae of breast cancer in China, which is not conducive to our understanding of the actual long-term rehabilitation needs of breast cancer survivors, also is unable to provide effective rehabilitation, to establish effective referral system, and to provide clinicians with the necessary knowledge of rehabilitation, which is critical for patients to receive timely rehabilitation and establish long-term health [28].

The main objective of this study was that we attempted to determine the incidence and prevalence of Arm Morbidity (AM) including lymphedema, reduced ROM of the shoulder, pain, muscle weakness and paresthesia among breast cancer survivors in China. The secondary objective was to assess the possible risk factors associated with the development of upper limb disease and to analyze the potential factors affecting the recovery of upper limb function.

Methods

Study design and participants

A cross-sectional study was conducted and all measurements took place in the department of rehabilitation medicine, Jing'an District Central Hospital, Shanghai. All participants should sign the written consents before participating in the study. The rehabilitation evaluation was conducted for breast cancer patients who came to the hospital for the first time from January 01st, 2017 to December 31st, 2020, and their functional status was obtained and their rehabilitation needs were collected. Patients who could not participate normally due to cognitive impairment, had a history of upper limb neuromuscular disease or congenital lymphedema before breast cancer diagnosis, were diagnosed with bilateral breast cancer, and did not agree to participate in this study were excluded.

Procedures and measures

Participants took a subjective questionnaire for demographic information, clinical characteristics mainly including Axillary Web Syndrome (AWS) and brachial plexus injury, pain, paresthesia, allodynia, and phantom sensations, and were measured for AM including lymphedema, pain, range of motion, and muscle strength by trained clinical research assistants. The training included attending a two-day workshop led by a certified rehabilitation therapist in China. The workshop included a comprehensive, illustrated assessment manual, field operations, and real-time feedback from trainers. Each clinical evaluation lasted approximately 1 h and a separate clinic was available for evaluation.

Demographic and clinical characteristics

Demographic information included sex, age, height and weight (used to calculate Body Mass Index (BMI)). Clinical information included cancer type, surgery type (mastectomy, modified radical mastectomy, breast-conserving surgery), lymph node dissection type (axillary, sentinel), numbers of positive nodes removed, treatment type (radiation, chemotherapy, hormonal therapy), and time of occurrence of sequelae, and be treated time.

The impairments measurements

Grip strength and ROM: Hand-grip strength test was performed as an indicator of overall strength. The hand grip strength was measured using J-Tech Grip Strength device (JTech Medical, Midvale, Utah). The tracker computerized grip dynamometer is a wireless grip device that provides a reliable grip force assessment. The units of it were displayed in kilograms of force. In previous studies, test-retest reliability of J-Tech equipment has been examined, and it was excellent at high Interclass Correlation Coefficient (ICC) value, which ranged from 0.954 to 0.973 [29]. And research assistant gave a description of the hand grip strength test procedure and performed 3 trials on the patients and calculated the mean of the 3 trials. In each trial, the participants rested for 15 sec. During each test, the grip force was pressed for 2 sec to 3 sec to ensure maximum grip strength. Measurements were taken in the standard position of the elbow at 90%, the forearm neutral, and the wrist in neutral deviation., and both hands were tested as described above. Grip strength restriction was defined as the difference in the force between the affected and unaffected sides.

A goniometer was used to measure shoulder flexion, extension, abduction, horizontal position-internal rotation and external rotation in an upright or sitting position. The movement was measured to a

sensation of pain or a degree that the patient's arm could no longer move. Full shoulder abduction starts with arms alongside your sides, palms facing forward and fingers pointing at your toes. In the coronal semicircle motion, move the arm until the hand is up and the fingers point to the ceiling. Complete shoulder flexion starts in the same position as abduction. In a sagittal semicircle motion, arms move until the hand is up and the fingers point to the ceiling. Shoulder extension begins with shoulder flexion, and in a sagittal semicircle motion, the arm moves backward to the maximum Angle. The starting position of horizontal position-internal rotation and external rotation is 90° abduction of the shoulder joint with elbow flexion parallel to the ground. Internal rotation occurs by moving the fingers down until they point to the floor, and external rotation occurs by moving the fingers up until they point to the ceiling. ROM restriction was defined as the difference in the degree of rotation between the affected and unaffected sides. The possible fractional range for both flexion and abduction are 0° to 180°. The possible e fractional range for extension is 0° to 60°. The possible fractional range for both horizontal position-internal rotation and external rotation 0° to 90°.

Lymphedema: Arm measurements were undertaken using a retractable Jobst non-stretched soft tape measure commencing at the midpoint of the ulnar styloid set as the 0 cm mark and then at 10 cm intervals up to 40 cm proximal to the ulnar styloid. To improve diagnostic sensitivity, we consider lymphedema to be present when the circumference difference measured at a single point is greater than 1 cm.

Pain: The Numerical Rating Scales (NRSs) are used to measure pain, which is a simple and common way to assess changes in pain intensity. With the NRS, participants were asked to rate their average pain intensity over the last 7 days by selecting a single number from 0 to 10. The repeatability of the Visual Analogue Scale (VAS) is good as can be seen by correlation coefficients ranging from 0.97 to 0.99 [30]. The correlation between the NRSs and VAS was statistically high (r=0.93) [31].

Sample size

The sample size was calculated based on reports of the incidence of impairments in other countries. Ninety-three patients were needed in each arm in order to achieve 90% power with a two-sided 5% significance level.

Data analysis

We described participants' demographic information, history of cancer treatment, incidence of sequelae, time of impairments occurrence and rehabilitation delay time. At the same time, the degree and extent of lymphedema, pain, limited range of motion and muscle strength, and paresthesia were described. Among them, frequencies and percentages were used for categorical variables, continuous variables used means and standard deviations, or medians and quartiles when the data is not normally distributed. Chi-square tests were used to analyze the factors influencing the occurrence of lymphedema, then a possible model was obtained by multivariate logistic regression analysis. Kruskal-Walli's test was used to analyze the factors influencing the severity of lymphedema, then a possible model was obtained by multivariate linear regression analysis. Multivariate logistic regression was used to analyze the factors influencing the occurrence of pain, shoulder mobility limitation, grip strength limitation and paresthesia. Statistical significance was determined with p values of <0.05, and all analyses were performed using SPSS version 25.0 (IBM SPSS Statistics, Armonk, NY, USA).

Ethical considerations

The Shanghai Jing'an District Central Hospital Ethics Committee approved this study. All participants gave written informed consent before data collection began.

Results

We recruited 169 patients for participation in this study from January 01st, 2015, to December 31st, 2021. Thirty-one of these patients did not meet the inclusion criteria. Of these, twenty-two of patients had rotator cuff injury prior to diagnosis, and nine had bilateral breast cancer. Therefore, the final population in the intent to analysis included 138 patients. The characteristics of the 138 remaining participants in the study are listed in Table 1. Most of the participants were aged 51 to 70, accounting for 65.9%. According to the Chinese BMI standard, 46.4% of the participants were in a normal criterion, 36.2% were overweight and 14.5% were obese. Infiltrating ductal were found in 84.1% of breast cancer survivors who seek rehabilitation. ALND was performed in 89.2% of patients. The numbers of lymph nodes dissected in 45.6% patients more than 15. There were 89.9% of patients received chemotherapy, 56.6% received radiotherapy and 62.3% received endocrine therapy. The sequelae were lymphedema (65.9%), pain (31.2%), shoulder ROM restriction (20.3%), grip strength restriction (21.7%) and paresthesia (11.6%). The participants had a 6.5% incidence of AWS and an 10.9% incidence of brachial plexus injury. Possible sequelae occurred within 28 months of breast cancer diagnosis in 74.6% of participants. After the occurrence of sequelae, 80.4% of the participants would try to seek relevant treatment within 0 to 20 months, while 19.6% of the participants did not find a way to face the unavoidable sequelae until 70+ months (Table 1).

Trends in the incidence of lymphedema, pain, shoulder ROM restriction, paresthesia, and decreased grip strength when participants first came for rehabilitation evaluation from 2017 to 2020 are shown in Figure 1. The prevalence of lymphedema, pain, Shoulder ROM restriction, paresthesia, and decreased grip strength were 31%, 13%, 13%, 1.1%, and 13% respectively in 2017. They were 72%, 23%, 15%, 2%, and 20% respectively in the order listed above in 2018. 85%, 41%, 19%, 7%, and 33% respectively in 2019, and 53%, 50%, 37%, 43%, and 30% respectively in 2020 (Figure 1a). Although there was no statistically significant difference (p=0.28), the incidence of pain in 0 to 28 months after treatment (35.0%) was higher than that in 29 to 70 months (21.4%) and 71+ months (19.0%). The incidence of Shoulder ROM restriction in 0 to 28 months after treatment (24.3%) was higher than that in 29 to 70 months (14.3%) and 71+ months (4.8%) (p=0.12). The incidence of paresthesia at 0 to 28 months after treatment (11.7%) was higher than that at 28 to 70 months (7.1%) and lower than that at 71+ months (14.3%) (p=0.82). The incidence of decreased grip strength in 0 to 28 months after treatment (22.3%) was higher than that in 71+ months (9.5%) and lower than that in 29 to 70 months (35.7%) (p=0.18). The incidence of lymphedema in 0 to 28 months after treatment (69.9%) was higher than that in 29 to 70 months (50.0%) and 71+ months (57.1%) (p=0.21) (Figures 1b-1f).

The arm circumference of participants at 10 cm, 20 cm, 30 cm and 40 cm above the wrist was more than 1 cm, respectively was [1.90 (0.40, 3.60)] cm, [1.50 (0.70, 3.40)] cm, [2.00 (0.55, 3.90)] cm and [1.30 (0.60, 3.15)] cm. Pain occurred mainly in the shoulder and possibly involved upper limb area (65.1%), and possibly in the surgical site, back and axillary area (34.9%), with a mean score of 5.00 (2.00,6.00). The limitation of shoulder ROM was manifested in

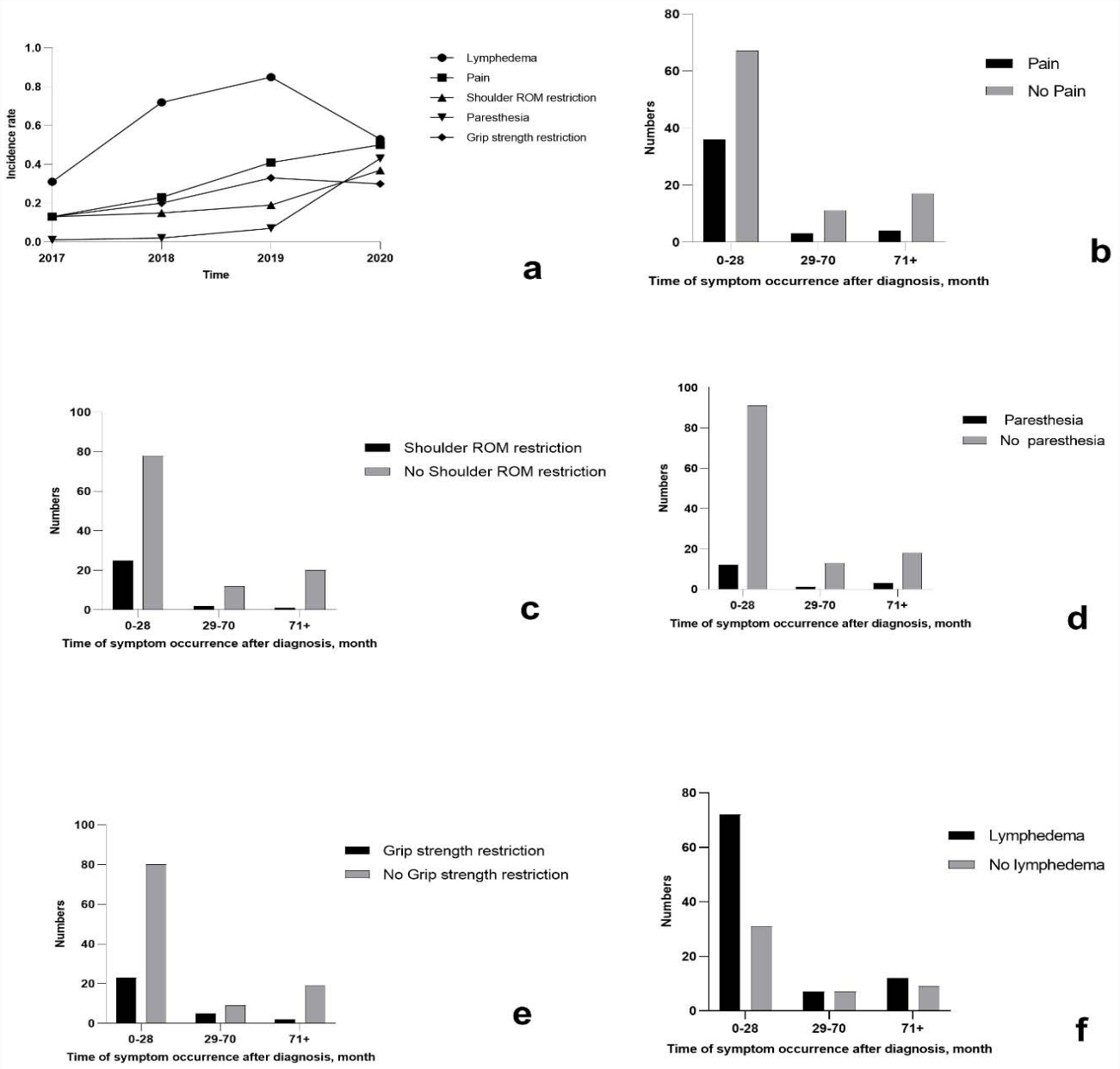

Figure 1: The Incidence of dysfunction and time of first occurrence after treatment in breast cancer patients from 2017 to 2020.

flexion difference of (39.50 ± 23.12)°, extension difference of (13.31 ± 10.16)°, abduction difference of (49.56 ± 27.84)°, horizontal internal rotation difference of [10.00 (0,39.75)]°, horizontal external rotation difference of [30.00(2.50,41.50)]°. The grip strength of the affected side also decreased by [3.50 (1.15,8.00)]°. The main paresthesia was numbness (47.4%), foreign body sensation and pulling sensation around the operative site and axilla (52.6%) (Table 2).

The multifactor linear regression equation was established by including chemotherapy, radiotherapy, age and delayed rehabilitation time. Radiotherapy significantly increased the degree of edema (B=1.64, t=3.06, p=0.003). Compared with patients with a recovery delay of 1 to 20 months, there was no significant difference in the degree of lymphedema in patients with a recovery delay of 21 to 69 months (B=0.44, t=0.54, p=0.587), while there was a significant increase in lymphedema in patients with a recovery delay of more than 70 months (B=2.20, t=2.65, p=0.010) (Figure 2).

Multi-factor logistic regression equation was established by including cancer type, lymph node operation method, number of lymph node metastasis, chemotherapy and radiotherapy. Invasive breast cancer was associated with occurrence of edema compared with carcinoma in situ (OR=6.18, 95% CI 1.85-20.72, p=0.003). Radiotherapy was associated with occurrence of edema (OR=0.28, 95% CI 0.13-0.61, p=0.001). Logistic regression equation was established for the occurrence of pain, shoulder ROM restriction, grip strength restriction and paresthesia. Postoperative pain of breast cancer was correlated with axillary web syndrome (OR=0.48, 95% CI 0.01-0.41, p=0.005) and brachial plexus injury (OR=0.27, 95% CI 0.08-0.84, p=0.025). There was a correlation between shoulder ROM restriction and brachial plexus injury (OR=0.27, 95% CI 0.08-0.84, p=0.025). The occurrence of grip strength restriction was correlated

Table 1: Characteristics of participants.

Characteristics	N	%
Sex		
Female	137	99.3
Male	1	0.7
Age at inclusion		
32-40	15	10.9
41-50	21	15.2
51-60	42	30.4
61-70	49	35.5
71-85	11	8
BMI		
<18.5	4	2.9
18.5-23.9	64	46.4
24-27.9	50	36.2
≥ 28	20	14.5
Cancer type		
Infiltrating ductal	116	84.1
Carcinoma in situ	15	10.9
Others	7	5
Lymph node procedure		
ALND only	95	68.8
SLND only	9	6.5
ALND and SLND	28	20.4
Does not apply	6	4.3
Numbers of dissected lymph nodes		
0-1	35	25.4
Feb-14	40	29
15-18	34	24.6
19+	29	21
Numbers of lymph node metastases		
0	86	62.3
1-2	19	13.8
3+	33	23.9
Chemotherapy		
Yes	124	89.9
No	14	10.1
Radiotherapy		
Yes	80	58
No	58	42
Endocrine therapy		
Yes	88	63.8
No	50	36.2
Lymphedema		
Yes	91	65.9
No	47	34.1
Pain		
Yes	43	31.2
No	95	68.8
Shoulder ROM restriction		
Yes	28	20.3
No	110	79.7
Grip strength restriction		
Yes	30	21.7
No	108	78.3
Paresthesia		
Yes	19	13.8
No	119	86.2
Axillary web syndrome		
Yes	9	6.5
No	129	93.5
Brachial plexus injury		
Yes	15	10.9
No	123	89.1
Time of symptom occurrence after diagnosis, month		
0-28	103	74.6
29-70	14	10.1
71+	21	15.3
Delayed rehabilitation time, month		
0-20	111	80.4
21-69	13	9.4
70+	14	10.2

Note: The time of delayed rehabilitation is from the onset of symptoms reported by the patient to the onset of rehabilitation

with brachial plexus injury (OR=40.53, 95% CI 8.40-195.65, p<0.001). Paresthesia was correlated with brachial plexus injury (OR=56.68, 95% CI 10.86-295.97, P<0.001) (Table 3).

Discussion

This study is one of the few cross-sectional studies on postoperative complications and related risk factors of breast cancer in China. The development of rehabilitation medicine in China is relatively late. It is commonly said that it began in the 1980s. Furthermore, the clinical and research of breast cancer rehabilitation is much later. From the medical side, firstly, the large medical institutions in some frontier cities in China are not equipped with breast cancer rehabilitation so far. Second, clinicians in the cancer department did not treat the possible sequelae after breast cancer surgery as a medical problem that must be dealt with. They do not recognize the need to assess and treat these sequelae, and do not inform patients of possible complications beyond recurrence after surgery and other treatments [32]. In addition, they are largely unaware of the referral if the patient develops sequelae during follow-up. From the patients, the patients can't independently identify these long-term chronic complications without prompting from the doctor, for example, they will regard the traumatic lymphedema as a short-term general swelling, believing that "it will get better on its own after a period of time" and thus missing the optimal time for treatment. At present, the common state of breast cancer-related rehabilitation in China is that treatment is likely to be delayed after the occurrence of symptoms, not even to mention how to prevent.

Table 2: Degree and extent of lymphedema, pain, limited range of motion and muscle strength, and paresthesia.

Measurements	N (%)#/Mean ± SD*/M (P25, P75)
The arm circumference measurement	
0 cm (wrist)	0.80 (0.30,1.35)
10 cm	1.90 (0.40,3.60)
20 cm	1.50 (0.70,3.40)
30 cm	2.00 (0.55,3.90)
40 cm	1.30 (0.60,3.15)
NRSs	
Position- Shoulder and upper limbs#	28, 65.1%
Chest and back and around axilla#	15, 34.9%
goal	5.00 (2.00,6.00)
Shoulder ROM restriction	
Flexion*	39.50 ± 23.12
Extension*	13.31 ± 10.16
Abduction*	49.56 ± 27.84
horizontal position-internal rotation	10.00 (0,39.75)
horizontal position- external rotation	30.00 (2.50,41.50)
Grip strength restriction	3.50 (1.15,8.00)
Paresthesia	
Numb#	9 (47.4)
Chest and armpit foreign body sensation and pulling	
Sensation#	10 (52.6)

Actually, Physical Therapy (PT) should begin when the patient is in the hospital preparing for surgery. Similar to the surgeon, PT should be thoroughly evaluated to check the patient's preoperative functioning and inform the patient of possible complications and precautions. Patients' functional status should also be assessed with PT follow-up during routine follow-up to surgery. We will investigate the current situation and needs of breast cancer survivors in China, and take the initiative to establish a mode of rehabilitation prevention -- chronic disease management that is suitable for China's medical system according to objective conditions.

Lymphedema occurred in 65.9% of participants in the study, pain occurred in 31.2%, Shoulder ROM restriction occurred in 20.3%, Grip strength restriction occurred in 21.7%, and paresthesia occurred in 13.8% of participants. Although most of these participants come from Shanghai, could not represent the entire China sequelae of breast cancer, However, if considered from the opposite perspective, Shanghai is China's super first-tier city, which can provide sufficient economic conditions and medical health care, but still has such a high incidence, so we can infer that the incidence of sequelae of breast cancer in other regions will not be low. We can see from the sequelae trend chart that the detection rate of lymphedema went from 30% in 2017 to 80% in 2019 to 60% in 2020; pain and paresthesia increased from 10%. The main reason may be that the development of lymphedema does affect the appearance, work and life of patients, so that they have to deal with the symptoms; However, when the continuous, low intensity of pain or numbness and foreign body sensation around the upper limbs of the affected side cannot directly affect the patients, they usually subjectively ignore this uncomfortable feeling, so they often tell PT “We don't have this feeling" in order to show that they are not exceptional. It may also be that after surgical treatment, the patients weren’t informed of the sequela that may occur in the following period of time, so didn’t treat these problems as symptoms that must be treated. This situation not only happens in China, there are studies that have concluded the common barriers to cancer rehabilitation, such as knowledge barriers including education concerning cancer rehabilitation, access barriers including time, money and transportation and adherence including fear of injury [28].

In this study, lymphedema was most severe at 10 cm and 30 cm from the wrist. There were two main "lines" of pain that patients complain about most. One was the surgical site and the affected shoulder extending to the arm, and the other was the affected axilla to the twelfth rib. The limited movement of shoulder joint was mainly manifested in forward flexion and abduction. There

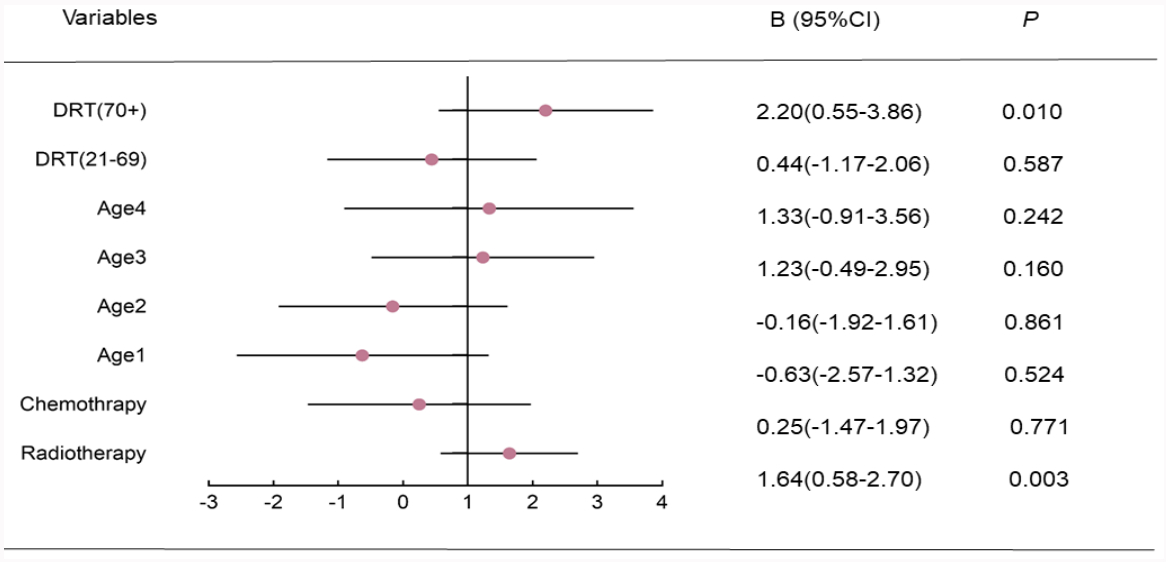

Figure 2: Multiple linear regression of influence on the severity of lymphedema.
DRT: Delayed Rehabilitation Time (month); Age 1:41 to 50 years’ old; Age 2:51 to 60 years’ old; Age 3:61 to 70 years’ old; Age 4: 70+years’ old
Note. R2=0.22, adjusted R2=0.17, F=4.10, p<0.001

Table 3: Logistic multifactor regression analysis for the occurrence of lymphedema, pain, shoulder ROM restriction, grip strength restriction and paresthesia.

	Lymphedema	Pain	Shoulder ROM restriction	Grip strength restriction	Paresthesia
	AOR (95% CI)	AOR (95% CI)	AOR (95% CI)	AOR (95% CI)	AOR (95% CI)
Cancer type					
Carcinoma *in situ*	6.18 (1.85,20.72)*				
Others	5.13 (0.88,29.83)				
Radiotherapy (yes)	0.28 (0.13,0.61)*				
Axillary web syndrome (Yes)		0.48 (0.01-0.41)*			
Brachial plexus injury (Yes)		0.27 (0.08-0.84)*	0.04 (0.01-0.15)*	40.53 (8.40,195.65)**	56.68 (10.86-295.97)**
Endocrine therapy (yes)			2.64 (0.98-7.14)		

P*<0.05, p**<0.001

was no significant decline in grip strength, except for severe nerve damage from chemotherapy or radiation. The main paresthesia was numbness and pulling. Previous studies had suggested that this series of symptoms can be classified as Chemotherapy-Induced Peripheral Neuropathy (CIPN), including numbness, foreign body sensation, tingling, weakness and pain [33]. Until now, it has been difficult to quantify the assessment, most of which was recorded by patients' self-report, which may lead to an estimate of the occurrence and severity of the symptom.

A large number of previous studies had found that age and BMI were risk factors for lymphedema, but they did not play a significant role in this study. This may be due to the wide age range of the cases we collected and the uniform distribution of the four body index levels. We also found that the type of cancer and the radiotherapy were major risk factors for lymphedema. This also requires further discussion on the classification of cancer types in the following studies. Risk factors affecting the severity of lymphedema were analyzed. Once lymphedema has occurred, older patients may develop higher grades of lymphedema. Treatment with chemotherapy and radiation also increases the degree of lymphedema. In addition to these normally studied factors, the concept of delayed recovery time was added and found to aggravate lymphedema, providing evidence that prevention and early recovery can reduce the occurrence of sequela.

In this study, pain, limited shoulder mobility, decreased grip strength, and abnormal sensation were found to be associated with brachial plexus injury. Brachial plexus injury after breast cancer treatment may be caused by chemotherapy, radiotherapy or surgical cutting of peripheral nerves. This suggests that these symptoms should be treated as peripheral nerve damage after breast cancer treatment and that these functional problems should be fully examined during evaluation.

We also found that many patients complained about their inability to do normal household chores or take care of their children or grandchild, but rarely brought up problems related to recreational activities, which was different from what had been reported in some European countries. In these studies, the patients would mention that the affected arm can't play golf or tennis/volleyball because it doesn't move well or can't be stretched too much as a precaution [34]. To some extent, this reflects the characteristics of Chinese social life. People, especially some middle-aged and elderly people, are used to focusing on making money and raising children, and they ignore their needs for social entertainment activities, which virtually lowers their requirements for the quality of life. This may also be a barrier to breast cancer rehabilitation.

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References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209-49.
2. Feng RM, Zong YN, Cao SM, Xu RH. Current cancer situation in China: Good or bad news from the 2018 Global Cancer Statistics? Cancer Commun (Lond). 2019;39(1):22.
3. DeSantis CE, Fedewa SA, Goding Sauer A, Kramer JL, Smith RA, Jemal A. Breast cancer statistics, 2015: Convergence of incidence rates between black and white women. CA Cancer J Clin. 2016;66(1):31-42.
4. Brookham RL, Cudlip AC, Dickerson CR. Quantification of upper limb electromyographic measures and dysfunction of breast cancer survivors during performance of functional dynamic tasks. Clin Biomech (Bristol, Avon). 2018;52:7-13.
5. Halsted WS. I. The results of radical operations for the cure of carcinoma of the breast. Ann Surg. 1907;46(1):1-19.
6. Nikkanen TA, Vanharanta H, Helenius-Reunanen H. Swelling of the upper extremity, function and muscle strength of shoulder joint following mastectomy combined with radiotherapy. Ann Clin Res. 1978;10(5):273-9.
7. Patey DH, Dyson WH. The prognosis of carcinoma of the breast in relation to the type of operation performed. Br J Cancer. 1948;2(1):7-13.
8. Madden JL. Modified radical mastectomy. Surg Gynecol Obstet. 1965;6(121):1221-30.
9. Shamley D, Srinanaganathan R, Oskrochi R, Lascurain-Aguirrebeña I, Sugden E. Three-dimensional scapulothoracic motion following treatment for breast cancer. Breast Cancer Res Treat. 2009;118(2):315-22.
10. Shamley DR, Srinanaganathan R, Weatherall R, Oskrochi R, Watson M, Ostlere S, et al. Changes in shoulder muscle size and activity following treatment for breast cancer. Breast Cancer Res Treat. 2007;106(1):19-27.

11. Crosbie J, Kilbreath SL, Dylke E, Refshauge KM, Nicholson LL, Beith JM, et al. Effects of mastectomy on shoulder and spinal kinematics during bilateral upper-limb movement. Phys Ther. 2010;90(5):679-92.

12. Borstad JD, Szucs KA. Three-dimensional scapula kinematics and shoulder function examined before and after surgical treatment for breast cancer. Hum Mov Sci. 2012;31(2):408-18.

13. Ludewig PM, Reynolds JF. The association of scapular kinematics and glenohumeral joint pathologies. J Orthop Sports Phys Ther. 2009;39(2):90-104.

14. Ebaugh D, Spinelli B, Schmitz KH. Shoulder impairments and their association with symptomatic rotator cuff disease in breast cancer survivors. Med Hypotheses. 2011;77(4):481-7.

15. Miaskowski C, Paul SM, Cooper B, West C, Levine JD, Elboim C, et al. Identification of patient subgroups and risk factors for persistent arm/shoulder pain following breast cancer surgery. Eur J Oncol Nurs. 2014;18(3):242-53.

16. Vidt ME, Daly M, Miller ME, Davis CC, Marsh AP, Saul KR. Characterizing upper limb muscle volume and strength in older adults: A comparison with young adults. J Biomech. 2012;45(2):334-41.

17. Sagen A, Kaaresen R, Sandvik L, Thune I, Risberg MA. Upper limb physical function and adverse effects after breast cancer surgery: A prospective 2.5-year follow-up study and preoperative measures. Arch Phys Med Rehabil. 2014;95(5):875-81.

18. Wisotzky E, Hanrahan N, Lione TP, Maltser S. Deconstructing postmastectomy syndrome: Implications for physiatric management. Phys Med Rehabil Clin N Am. 2017;28(1):153-69.

19. Hamood R, Hamood H, Merhasin I, Keinan-Boker L. Chronic pain and other symptoms among breast cancer survivors: Prevalence, predictors, and effects on quality of life. Breast Cancer Res Treat. 2018;167(1):157-69.

20. Waltho D, Rockwell G. Post-breast surgery pain syndrome: Establishing a consensus for the definition of post-mastectomy pain syndrome to provide a standardized clinical and research approach - a review of the literature and discussion. Can J Surg. 2016;59(5):342-50.

21. Terao Y, Taniguchi K, Fujii M, Moriyama S. Postmastectomy radiation therapy and breast reconstruction with autologous tissue. Breast Cancer. 2017;24(4):505-10.

22. Johansen S, Fosså K, Nesvold IL, Malinen E, Fosså SD. Arm and shoulder morbidity following surgery and radiotherapy for breast cancer. Acta Oncol. 2014;53(4):521-9.

23. Levy EW, Pfalzer LA, Danoff J, Springer AB, McGarvey C, Shieh C, et al. Predictors of functional shoulder recovery at 1 and 12 months after breast cancer surgery. Breast Cancer Res Treat. 2012;134(1):315-24.

24. Wernicke AG, Goodman RL, Turner BC, Komarnicky LT, Curran WJ, Christos PJ, et al. A 10-year follow-up of treatment outcomes in patients with early-stage breast cancer and clinically negative axillary nodes treated with tangential breast irradiation following sentinel lymph node dissection or axillary clearance. Breast Cancer Res Treat. 2011;125(3):893-902.

25. Monleon S, Ferrer M, Tejero M, Pont A, Piqueras M, Belmonte R. shoulder strength changes one year after axillary lymph node dissection or sentinel lymph node biopsy in patients with breast cancer. Arch Phys Med Rehabil. 2016;97(6):953-63.

26. Yang JD, Huh JS, Min YS, Kim HJ, Park HY, Jung TD, et al. Physical and functional ability recovery patterns and quality of life after immediate autologous latissimus dorsi breast reconstruction: A 1-year prospective observational study. Plast Reconstr Surg. 2015;136(6):1146-54.

27. Boquiren VM, Hack TF, Thomas RL, Towers A, Kwan WB, Tilley A, et al. A longitudinal analysis of chronic arm morbidity following breast cancer surgery. Breast Cancer Res Treat. 2016;157(3):413-25.

28. Stubblefield MD. The underutilization of rehabilitation to treat physical impairments in breast cancer Survivors. PM R. 2017;9(9S2):S317-23.

29. Clerke AM, Clerke JP, Adams RD. Effects of hand shape on maximal isometric grip strength and its reliability in teenagers. J Hand Ther. 2005;18(1):19-29.

30. Williamson A, Hoggart B. Pain: A review of three commonly used pain rating scales. J Clin Nurs. 2005;14(7):798-804.

31. Thong I, Jensen M P, Miró J, Tan G. The validity of pain intensity measures: What do the NRS, VAS, VRS, and FPS-R measure? Scand J Pain. 2018;18(1):99-107.

32. Rafn BS, Midtgaard J, Camp PG, Campbell KL. Shared concern with current breast cancer rehabilitation services: A focus group study of survivors 'and professionals' experiences and preferences for rehabilitation care delivery. BMJ Open. 2020;10(8):1-10.

33. Brown TJ, Sedhom R, Gupta A. chemotherapy induced peripheral neuropathy. JAMA Oncol. 2019;5(5):750.

34. Lattanzi JB, Giuliano S, Meehan C, Sander B, Wootten R, Zimmerman A. Recommendations for physical and occupational therapy practice from the perspective of clients undergoing therapy for breast cancer-related impairments. J Allied Health. 2010;39(4):257-64.