

## Prospective Study of Postoperative Pain Syndrome in Patients with Breast Cancer and its Related Factors

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Received date: August 27, 2016; Accepted date: September 19, 2016; Published date: September 22, 2016

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### Abstract

**Background:** Surgery is usually the first treatment for breast cancer which is followed by some complications such as chronic pain. Post mastectomy pain syndrome (PMPS) is a common complication among breast cancer survivors and is considered as a chronic neuropathic pain in the side of surgery which persists more than six months. The exact mechanisms and related risk factors of the chronic pain after breast surgery are unknown. The aim of this study is to investigate the epidemiological characteristics of postoperative pain syndrome in Chinese breast cancer patients, and to analyze the related risk factors.

**Methods:** A prospective cohort study of 202 female breast cancer patients undergoing elective breast surgery for a period of 6 months follow-up survey. The incidence rate of pain in patients with chronic pain was assessed by the self-rating scale of ID. Pain and 16 related risk factors were statistically analyzed.

**Results:** A prospective cohort study of 202 female breast cancer patients undergoing elective breast surgery for a period of 6 months follow-up survey. The incidence rate of pain in patients with chronic pain was assessed by the self-rating scale of ID. Pain and 16 related risk factors were statistically analyzed.

**Conclusions:** PMPS occupies a certain proportion in breast cancer patients after surgery. Age and psychological abnormalities associated with preoperative breast cancer patients may undergo PMPS. It is possible to have a certain significance to choose the operation mode of the trauma, the psychological intervention before the operation and the management of the acute pain after the operation to prevent the PMPS.

**Keywords:** Post-mastectomy pain syndrome; Chronic pain; Neuropathic pain

### Materials and Methods

#### General information

**Object of investigation:** Select female patients with breast cancer, ASA I~III, which operate elective breast surgery from May 2015 to May 2016 in Shanghai east Hospital. All patients had clinical and pathological diagnosis of breast cancer before surgery, and there was no cognitive impairment. All informed and agreed to accept the investigation of the diagnosis.

#### Survey methods

**Preoperative visit to the patients and record:** 1. General conditions: name, age, height, weight, BMI, marital status, educational level. 2. Psychological assessment: anxiety and Depression Rating Scale (evaluation criteria: HAD scale). 3. Previous history of breast surgery, whether the patient has had or is now suffering from chronic pain, If combined with other comprehensive pain. The syndrome and pain medications, and the type and dose of drug.

- Record the patient's tumor site, surgical approach, whether the axillary lymph node dissection, the use of non-steroidal anti-inflammatory drugs (NSAIDs), whether with postoperative pain pump.

### Introduction

Post-mastectomy pain syndrome (PMPS) is a chronic type of breast cancer after operation. First reported by wood in last 70's century [1]. With the near over the decades, the importance of PMPS and research increased, found that PMPS occurring in the clinical occupies a considerable proportion, and seriously affect the breast physiology, psychology and quality of life of cancer patients after surgery.

According to foreign literature, the incidence of PMPS in 10%-80%, and symptoms can be sustained for 9 years [2], and the quality of life of PMPS patients was significantly lower [2-4]. The specific cause of PMPS is not completely clear.

Indeed, the present study is consistent with the multiple factors like the Brachial nerve injury, preoperative anxiety and depression, postoperative mild to moderate acute Pain, radiotherapy and chemotherapy, etc. The treatment measures and effects of PMPS are confirmed by large sample clinical trials. Abroad on the epidemiology of PMPS and long-term follow-up of more, but domestic researches have not been sufficient for PMPS, there is no relevant systematic investigation.

- Record the NRS score of 24 h after extubation in patients. Patients were followed up and recorded at 3 months and 6 months after operation respectively: 1. the time, location, nature, characteristics, and the degree of pain of postoperative pain (NRS) 2. Whether the use of analgesics, as well as the types and doses 3. Radiotherapy and chemotherapy; 4. Tumor recurrence or metastasis.
- To send ID Pain scale of patients with chronic pain after operation, to have their complete and return.

### Criteria for diagnose PMPS

According to the International Association for the study of pain (IASP) chronic pain standards, the PMPS of this study should be consistent with the: 1. The time of pain was more than that of normal tissue after breast surgery (3 months) 2. The pain site is located on the same side of the armpit, arm, shoulder or chest wall.

### Statistical methods

Using SPSS 13.0 for statistical analysis, the relationship between PMPS and related variables was analyzed by using two classification variables Logistic regression. Measurement data two mean comparison

with f test, count data two overall rate difference of inference using  $\chi^2$  test.

## Results

### Epidemiological characteristics of PMPS

In this study, 202 female patients with breast cancer were included in the study. All patients were followed up for 6 months. To the end of the survey there are 2 cases of loss of follow-up, the actual completion of 200 cases. Respondents aged 22 to 82 years old, average age  $52 \pm 11.6$  years old of the 200 patients, 42 had postoperative chronic pain. Sent 42 patients with pain in the mail Pain-ID scale, the actual recovery of 42 copies, and all for the effective answer.

Statistics on the general situation of the patients interviewed (Table 1). In 42 patients with PMPS, the highest pain was in the ipsilateral axillary (18 cases, 43%), and the rest were in the same side of the chest wall (11 cases, 26%), with the same side arm (10 cases, 24%) and the other parts (3 cases, 7%). In patients with pain, Pain-ID scale score of 4 to 5 in 8 cases (19%), 2 to 3 points in 12 cases (29%), a score of 1 in 19 cases (45%), Scores of 0 or -1 in 3 cases (7%).

PMPS patients			Non-PMPS patients		Total
Age(Years)	Number	Percentage (%)	Number	Percentage (%)	Number
~30	3	50	3	50	6
30~49	26	31	58	69	84
50~69	12	12.8	82	87.2	94
70~	1	6.2	15	93.8	16
Marital status					
Married	39	20.7	149	79.3	188
Unmarried	3	25	9	75	12
Education background					
Primary school	5	20.8	19	79.2	24
High school	27	21.8	97	78.2	124
Undergraduate	10	19.2	42	80.8	52

**Table 1:** Demographic characteristics of PMPS and Non-PMPS patients.

Nature of pain for more numbness of 33 patients (79%), burning like 21 cases (50%), followed by the rest of acupuncture or needle like (17 cases, 40%), electrical (12 cases, 29%). Clothes or linens friction will increase the pain (allodynia) of 11 cases (26%).

In the telephone follow-up of patients found that with a certain proportion of patients appeared in other symptoms of pain, such as weak in 6 cases (14%) and a throbbing pain in 4 cases (10%), the

phantom pain (1 case, 2%). In severe pain intensity (NRS score  $\geq 4$ ) of 5 cases (12%)

3 patients took their own pain medication, 5 patients received physical therapy. The time of the pain occurred from months to 4 months after the operation, and the onset of the pain was characterized by continuous or intermittent episodes (Table 2).

Time of onset of pain	Number	Percentage (%)
Immediate	19	45
Less than one month	11	26

1~3 months	8	19
More than 3 months	4	10
<b>Frequency of pain</b>		
Continuous	12	29
Daily	17	40
Weekly	10	24
Monthly	3	7

**Table 2:** Onset and frequency of PMPS.

**PMPS risk factor analysis**

**Single factor analysis:** by single factor analysis found that between the two groups in the difference has statistical significance of the

variables age, preoperative anxiety and depression, acute pain, axillary lymph node dissection, preoperative chemotherapy, a total of five Statistical results (Tables 3 and 4).

Variables	PMPS group	Non-PMPS group	t value	p value
Age(Years)	47.0 ± 11.5	53.4 ± 12.0	3.057	0.003
Height(cm)	161.1 ± 6.2	160.3 ± 4.9	0.947	0.345
Weight(kg)	63.2 ± 9.1	63.0 ± 9.7	0.122	0.903
BMI	24.3 ± 3.2	24.6 ± 4.0	0.374	0.709
Degree of postoperative acute pain	1.9 ± 1.7	1.3 ± 1.2	1.974	0.054

**Table 3:** Statistical results.

Variables	Classification	PMPS	Non-PMPS	χ <sup>2</sup> value	p value
		Number	Number		
Marital status	Married	39	149	0.123	0.726
	Unmarried	3	9		
Education Background	Primary school	5	19	0.143	0.931
	High school	27	97		
	Undergraduate	10	42		
Preoperative anxiety and depression	Yes	8	7	8.221	0.004
	No	34	151		
Other pain syndrome	Yes	9	2	1.427	0.232
	No	33	136		
Location of tumor	Upper quadrant	33	109	1.48	0.224
	Lower quadrant	33	49		
Type of surgery	Radical surgery	39	144	0.002	0.965
	Conservative and other type of surgery	3	14		
Axillary lymph node dissection	Yes	38	121	3.93	0.047

	No	4	37		
NSAIDS drugs during surgery	Yes	23	82	0.109	0.741
	No	19	76		
Pre-operative chemotherapy	Yes	11	31	4.108	0.043
	No	31	137		
Post-operative chemotherapy	Yes	35	118	1.381	0.24
	No	7	40		
Post-operative radiotherapy	Yes	1	6	0.97	0.657

**Table 4:** Statistical results.

The establishment of regression model: univariate analysis a larger role in the five variables into binary variable logistic regression analysis model, selected variables of significant level of 0.05, 0.10 to eliminate variables of significant level. Candidate regression equation of variable

has four, respectively, age, preoperative anxiety and depression, axillary lymph node dissection, NRS score, indicating that in the pathogenesis of PMPS above four factors the influence PMPS independent risk factors (Table 5).

Variables coefficient	Partial regression	SE	Wald $\chi^2$ value	p value	OR value
Age	0.042	0.017	6.382	0.012	1.043
Preoperative anxiety and depression	1.944	0.615	9.99	0.002	4.143
Axillary lymph node dissection	1.318	0.61	4.633	0.031	2.268
Degree of postoperative acute pain	0.323	0.134	5.806	0.016	1.724

**Table 5:** Estimation of regression coefficient with statistical results and OR-value.

## Discussion

According to foreign reports, the occurrence of PMPS rate from 10% ~ 80%, leading to this difference may be due to a variety of: different tools and assessment methods such as patient selection range of different; measuring the degree of pain, duration of follow-up was different. In the present study, the incidence of PMPS was 21%; the highest incidence of pain was in the ipsilateral axillary (18 cases, 43%); the highest proportion nature of pain in the patients is numbness (33 cases, 79%). A total of 20 (48%) patients' ID-Pain score greater than or equal to 2, indicating a considerable proportion of patients may appear neuropathic pain.

The study also found that a considerable number of PMPS patients did not go to the hospital, a small number of people taking the pain medication, or accept the physical therapy, such as massage, hyperthermia, etc. And foreign research reports about 20% of PMPS patients go to the hospital, other PMPS patients are mostly self-medication and other treatment [5-7]. It shows that the cognitive ability of patients with PMPS is not enough in China, which suggests that in the future, we should strengthen the propaganda and education, so that the breast cancer patients have more understanding and understanding of PMPS. The research on etiology of PMPS show that intraoperative nerve injury is a major risk factor for the incidence and other influencing factors Includes young, type of surgery, axillary lymph node dissection, adjuvant chemotherapy and radiotherapy and

postoperative acute pain, psychological factors such as preoperative anxiety.

Age is one of the most dangerous factors in the literature [2,6-10]. The results of this study are consistent with the majority of foreign literatures, and the incidence of PMPS is increasing with the decreasing of age. The average age of PMPS patients was  $47.4 \pm 11.5$  years old, the average age of non PMPS patients was  $53.4 \pm 12$  years old, and the difference was statistically significant ( $P < 0.05$ ). Consider may be related to the following reasons [3]: 1. The young patients were more sensitive to the nerve injury, 2. The axillary dissection was more extensive. 3. The premenopausal female breast cancer incidence rate is high. 4. Young patients are more prone to anxiety, and therefore have a lower threshold for all kinds of bad feelings.

Acute pain after surgery is widely recognized as an independent risk factor for PMPS [10-13]. The study found: after operation of moderate degree and above with a total of 17 acute pain (NRS score greater than or equal to 4 points), in which patients with PMPS accounted for 7 cases, patients with non PMPS in 10 cases. Although postoperative acute pain score of all patients was not high ( $1.37 \pm 1.45$ ), it was a mild pain level, but there were significant differences in pain scores between PMPS patients and non PMPS patients ( $P < 0.05$ ).

Psychological factors, especially anxiety and depression before the operation also played a role in the occurrence of PMPS. The study by Katz [14] found that preoperative anxiety was significantly associated

with postoperative acute pain, which may lead to the occurrence of PMPS.

In breast cancer surgery during the treatment of axillary dissection has been a routine operation for breast cancer surgery. But much of the literature shows that axillary lymph node dissection is closely related with the occurrence of PMPS [8,15], mainly because in axillary lymph node dissection process will injury intercostobrachial nerve. Reported 80% ~100% of the patients with breast resection received axillary lymphadenectomy intercostobrachial nerve damage [16-18]. The results of this study showed that the relative risk of PMPS in patients with axillary lymph node dissection was not more than that of the Patients with lymph node dissection were 1.268 times as large as. Therefore, the use of sentinel lymph node biopsy compared with traditional axillary lymph node dissection is likely to reduce the risk of injury to the arm and axillary, chest wall sensory nerve, thereby reducing the risk of PMPS.

Operation mode is also one of the influencing factors of PMPS. Foreign literature reported that breast conserving surgery than breast cancer radical mastectomy or modified radical mastectomy with high incidence of PMPS, the use of prosthesis implantation of breast reconstruction than the breast reconstruction without prosthesis PMPS incidence rate. In the present study, the majority of breast cancer patients were treated by radical mastectomy, only 14 cases (7%) with breast conserving surgery, 3 cases (7%) were treated with prosthesis placement. In order to reduce the statistical bias, breast conserving surgery and breast reconstruction with prosthesis implantation were combined, but after single factor analysis, there was no significant difference in the incidence of PMPS. The reason may be due to the limited number of cases in this survey, the number of cases of various types of cases, so that the results appear biased. Another possible reason is that the current breast surgeons pay more attention to neural protection during the operation. At present domestic and foreign scholars are of the view that intraoperative integrity preserving intercostobrachial nerve does not affect the radical operation, also does not increase the likelihood of local recurrence in the axillary [19].

## Conclusion

PMPS has a certain proportion in breast cancer patients after operation. Correlation analysis of risk factors for PMPS suggests that clinicians, young and with preoperative psychological abnormality of breast cancer patients have PMPS. In addition, as far as possible to choose a relatively small trauma surgery, preoperative psychological intervention and postoperative acute pain management for the prevention of PMPS may have certain significance.

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