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Original article

Post-mastectomy pain syndrome: Incidence and risks

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ABSTRACT

Background: Post-mastectomy pain syndrome is defined as a chronic pain that persists beyond the normal healing time of 3 months. It is considered a neuropathic condition that arises after surgery for breast cancer.
Aim: To evaluate the incidence and risk factors of pain syndromes in patients undergoing surgical treatment of breast cancer in the National Cancer Institute.
Methods: This study is a prospective cohort of women undergoing surgical treatment for breast cancer from September 2008 to June 2009, followed up until 6 months postoperatively.
Results and conclusions: One hundred seventy-four women were examined. The mean age was 58 years. The incidence of pain syndrome was 52%. Younger women (<40 years) and those who were submitted to axillary lymph node dissection (with more than 15 lymph nodes excised) have shown a significantly increased risk of pain syndrome after surgery for breast cancer (relative risk (RR) = 5.23 95% confidence interval (CI): 1.11–24.64) and (RR = 2.01 95% CI: 1.08–3.75).

Pain can be defined as "an unpleasant sensorial and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."[1] Post-mastectomy pain syndrome (PMPS) is defined as chronic pain for over a 3-month-period. It is caused either by primary lesion or by dysfunction in the nervous system. It is considered a neuropathic condition which arises after surgical treatment for breast cancer and can occur due to intercostobrachial nerve (ICBN) lesion, neuroma, lesions of other nerves or the phantom breast pain. PMPS is different from other painful syndromes because it is typically localised to the anterior or lateral region of thorax, axillary and/or medial upper arm, causing burning pain, shooting pain, pressure sensation or numbness.[2–6]

The objective of this study is to assess the incidence and risk factors of pain syndromes in patients who have undergone surgical treatment of breast cancer at the National Cancer Institute, Brazil.

Materials and methods

This study deals with a prospective cohort of women who underwent surgical treatment for breast cancer at Cancer Hospital III/National Cancer Institute, Brazil, from September 2008 to June 2009.

Patients who had experienced any of the following were excluded from the study: pain caused by previous ostheomioarticular lesion at preoperative assessment, immediate reconstruction, bilateral breast cancer, difficulty in answering questions and clinical stage IV cancer. Eligible women were informed about the objectives and evaluation. Participants signified their willingness to be part of the study by signing an agreement, according to resolution 196/96. This study obtained approval from the National Cancer Institute, Ethics Committee under number 015/08.

Data were gathered through physiotherapeutic assessments at a previously established routine in service from 45 days preoperatively to 6 months postoperatively.

Pain syndrome after 6 months of surgical treatment for breast cancer was defined by the presence of one of the following

Abbreviations: AWS, Axillary web syndrome; CI, Confidence interval; CT, Chemotherapy; HMT, Hormone therapy; ICBN, Intercostobrachial nerve; PMPS, Post-mastectomy pain syndrome; RR, Relative risk; RT, Radiotherapy.

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complications: intercostobrachial pain (hyperaesthesia perception related to tactile stimulus at the internal area of the arm or axillary homolateral to treatment); neuroma (report of pain in the surgical scar when submitting to local percussion test); and phantom breast pain (reported by a patient who underwent mastectomy describing an unpleasant sensation of breast presence as pin-prick, burning or torsion).

In this study the socio-demographic characteristic of patients, type of treatment, tumour aspects and postoperative complications were collected.

To calculate the sample, a 15% incidence of painful syndrome was considered. With 95% confidence interval (CI), keeping 80% of power, it would be necessary to include 164 women.

A descriptive analysis of the studied population was accomplished through the central tendency measures for the continuous variables and for absolute and relative values for the categorical variables. In order to assess the association (relative risk) between the main conclusion and the independent variables, a bivariate analysis was accomplished, considering significant CI of 95%. In order to create the final model of risk, statistically significant variables were analysed by means of logistic regression (enter method).

Results

In this study, 203 patients were included. In the 45-day evaluation, four were excluded because of surgical alteration, conduct that was proposed previously. There were six losses to follow-up, in which one had suffered stroke, three by discontinuing the oncologic treatment and two because of death. At the 6-month evaluation, there were two exclusions due to advanced tumoural disease that led to treatment at Palliative Care Unit/National Cancer Institute and 17 losses to follow-up: 14 by discontinuing the treatment and three because of death. In the end, the study comprised 174 women.

The average age of women who were included in the study was 58 years (SD = 13). In relation to nutritional status, the average body mass index was 28 (SD = 5), in which 72.3% of women were classified as overweight or obese.

In relation to socio-demographic variables, 52.3% of patients lived with their partners, 46.6% were illiterate or had incomplete primary schooling, and 52.3% presented unstable employment; 59.1% stated that housework is their main function and most of them (96.8%) declared having right limb as the dominant one (right-handed). In relation to psychological profile, 75.1% of all women presented alteration in mood (anxious, depressed mood or anguished) at the first psychological assessment. When evaluating factors which are associated with pain syndrome, women under 40 years of age showed 1.67 times more risk in relation to the ones who were older (relative risk (RR) = 1.67; 95% CI: 1.27–2.21). Other demographic variables are not statistically significant (Table 1).

At preoperative evaluation, the most frequent complication was subjective sensation of lymphoedema at upper limb homolateral to breast cancer (8.3%). At bivariate analysis, these women have presented 1.59 more risks of proceeding with pain syndrome in relation to those who have not referred to subjective lymphoedema (RR = 1.59; 95% CI: 1.18–2.14) (Table 2).

In relation to the treatment, 73.6% women underwent mastectomy and 67.6% to axillary lymphadenectomy with an average number of 13 lymph nodes being removed (DP = 9.2). In relation to neo-adjuvant oncologic treatment, 26.9% of all women were submitted to chemotherapy, 4.1% to radiotherapy and 10.9% to hormone therapy. As supplementary treatment for evaluating the 6-month follow-up, 23.5% were taking chemotherapy, 19.3% were taking radiotherapy and 46.5%, hormone therapy; 34.2% had completed chemotherapy and 17.2% radiotherapy once. Variables statistically associated with pain syndrome were the number of lymph nodes removed (RR = 1.40; 95% CI: 1.06–1.86) and the accomplishment of biopsy of sentinel lymph node (RR = 0.58; 95% CI: 0.40–0.86) (Table 3).

When considering tumour characteristics, 53.4% of all patients presented tumour at right breast, with an average two lymph nodes positive (DP = 4.7); 44.6% of patients had shown at least one lymph node positive and advanced staging (≥IIB) that was also present in 44.6% women. During the follow-up of the study, 2.6% presented local relapse of the disease and 5.7% evolved to metastasis. No variable related to the characteristics of the tumour presented statistically significant association (Table 4).

The first ambulatory assessment was carried out at the 50th day postoperatively on average (DP = 23.2), in which 112 women (61.2%) presented pain syndrome: 61.3% of women presented altered superficial tenderness when touching the internal area of arm or axillary, 6.1% patients presented phantom breast pain, 3.3% presented Tinel test positive, 28.1% presented palpable string in

Table 1
Frequency and bivariate analysis between painful syndromes and independent variables related to demographic feature.

Variable	Painful syndrome		RR	CI 95%	*P* value
	Yes	No			
Age					
Up to 39 years	11	02	1.67	1.27–2.21	0.02
≥40 years	81	79			
Stable union					
Yes	44	45	0.87	0.66–1.16	0.37
No	48	37			
Body mass					
Obesity	27	27	0.93	0.68–1.28	0.7
Overweight and adequate	61	53			
Schooling					
Poor	37	41	0.83	0.62–1.11	0.22
Average and high	55	41			
Employment bond					
Unstable	54	38	1.23	0.95–1.69	0.13
Stable	38	44			
Occupation					
At home	51	51	0.88	0.66–1.16	0.44
External job	41	31			
Psychological profile					
Alterated	67	61	0.96	0.70–1.32	0.86
Easy	25	21			
Dominant hand					
Right handed	85	76	1.06	0.47–2.38	0.61
Left handed	3	3			

RR = Relative Risk; CI = Confidence Interval.

Table 2
Frequency and bivariate analysis between painful syndromes and independent variables related to preoperative assessment.

Variable	Painful syndrome		RR	CI 95%	*P* value
	Yes	No			
Pain on stricken side					
Yes	02	01	1.27	0.56–2.85	1.00
No	90	81			
Subjective lymphoedema					
Yes	12	03	1.59	1.18–2.14	0.03
No	80	79			
Movement restriction					
Yes	01	00	–	–	–
No	91	82			
Axillary area syndrome					
Yes	01	01	0.94	0.23–3.80	1.00
No	89	79			

RR = Relative Risk; CI = Confidence Interval.

Table 3
Frequency and bivariate analysis between painful syndromes and independent variables related to treatment.

Variable	Painful syndrome		RR	CI 95%	*P* value
	Yes	No			
Neo-adjuvant CT					
Yes	29	17	0.78	0.59–1.04	0.12
No	63	65			
Surgery					
Mastectomy	71	56	0.87	0.66–1.16	0.23
Conservative	21	26			
Removed lymph nodes					
>15	49	29	1.40	1.06–1.86	0.02
Up to 15	43	53			
Adjuvant CT					
Yes	54	42	1.19	0.88–1.61	0.28
No	34	38			
Current CT					
Yes	19	19	0.94	0.66–1.35	0.85
No	69	61			
Adjuvant RT					
Yes	37	29	1.09	0.82–1.45	0.64
No	55	52			
Current RT					
Yes	22	13	1.24	0.91–1.68	0.26
No	70	68			
Adjuvant HMT					
Yes	44	36	0.95	0.72–1.26	0.76
No	46	42			
Axillary approach					
BLS	20	36	0.58	0.40–0.86	0.00
LA	72	46			

RR = Relative Risk; CI = Confidence Interval; CT = Chemotherapy; RT = Radiotherapy; HMT = Hormone Therapy.

arm or axillary which confirmed axillary web syndrome (AWS) and 24.3% related pain at shoulder tests.

The final follow-up was carried out in an average of 8 months after surgery (DP = 1.3), and 52.9% have presented pain syndrome: 52.6% complained hyperaesthesia when touching the internal area of arm or axillary, 3.2% related pain on the phantom breast, 1.3% were Tinel test positive, 17.4% of women still presented AWS and 27.2% complained of pain at the shoulder tests.

The patients studied showed acute scar alterations: necrosis (19.7%), haematoma (7.4%), infection (11.8%), seroma (38.5%) and dehiscence (30%). Subjective oedema sensation was described by 38.4% in the first evaluation and 29.5% in the continuance of 6 months. When oedema was evaluated in objective ways, taking into consideration, volume alteration of the limb homolateral to the surgery was higher than 200 ml when compared to contralateral; patients have presented 3.1% during the first following evaluation and 4.7% in the second one. There was no alteration in the frequency of late scar alterations (adherence, fibrosis and retraction) in the periods of follow-up (60.9% and 59.3%, respectively). However, in relation to joint restriction, there was a reduction of incidence during the follow-up (23% and 3.4%, respectively). In evaluating treatment complications and the occurrence of pain syndrome, women having tissue necrosis showed 40% less chances of developing pain syndrome (RR = 0.60 95% CI: 0.36–0.99). Subjective lymphoedema (RR = 1.54; 95% CI: 1.18–1.20) and the presence of AWS (RR = 1.70; 95% CI: 1.32–2.18) (Table 5) were identified as risks.

The final risk model, after controlling confounding and interaction variables, has concluded that younger women (<40 years) present a higher 5.22 risk (RR = 5.23; 95% IC: 1.11–24.64) and those submitted to axillary approach with more than 15 removed lymph nodes presented a 2.01 higher risk (RR = 2.01; 95% CI: 1.08–3.75) of developing pain syndrome after the surgical treatment for breast cancer.

Table 4
Frequency and bivariate analysis between painful syndromes and independent variables related to tumour.

Variable	Painful syndrome (%)		RR	CI 95%	*P* value
	Yes	No			
Tumour side					
Right	45	46	0.87	0.66–1.16	0.36
Left	47	36			
Lymph node profile					
Positive	43	34	1.10	0.84–1.46	0.54
Negative	49	48			
Positive lymph nodes					
>3	18	22	0.67	0.44–1.00	0.07
1 and 2	25	12			
Staging					
Advanced ≥ 2B	40	36	0.99	0.75–1.32	1.00
Early ≤ 2A	52	46			
Local relapse					
Yes	02	03	1.17	0.39–3.48	0.56
No	60	115			
Metastasis					
Yes	02	03	0.75	0.25–2.20	0.67
No	90	78			

RR = Relative Risk; CI = Confidence Interval.

Discussion

After a 6-month follow-up assessment, the incidence of pain syndrome was 52.9%. Carpenter et al. (1998)[6] evaluated their

Table 5
Frequency and bivariate analysis between painful syndromes and independent variables related to complication.

Variable	Painful syndrome		RR	CI 95%	*P* value
	Yes	No			
Necrosi					
Yes	11	21	0.60	0.36–0.99	0.03
No	80	60			
Haematoma					
Yes	06	07	0.86	0.47–1.59	0.77
No	85	74			
Infection					
Yes	10	10	0.93	0.59–1.48	0.81
No	81	70			
Seroma					
Yes	36	28	1.07	0.81–1.42	0.64
No	54	49			
Dehiscence					
Yes	26	26	0.91	0.66–1.25	0.61
No	61	50			
Subjective oedema					
Yes	36	15	1.54	1.18–1.20	0.00
No	56	66			
Oedema vol > 200 mL					
Yes	03	06	0.62	0.24–1.57	0.31
No	89	76			
Scar alteration					
Yes	53	46	1.07	0.79–1.45	0.75
No	34	34			
Axillary web syndrome					
Yes	24	06	1.70	1.32–2.18	0.00
No	67	75			
Joint restriction					
Sim	03	03	0.94	0.42–2.13	1.00
No	89	79			
Positive shoulder tests					
Yes	27	19	1.13	0.84–1.52	0.49
No	64	59			

RR = Relative Risk; CI = Confidence Interval.

patients after a 3-month treatment and they have verified prevalence of syndrome in 27% of patients, Vilholm et al. (2008)[7] observed a 24% prevalence at 1.5 years postoperatively; such differences can be justified by the interval of evaluation and method. In our study, we accomplished physical evaluation of patients. Telephone interviews were carried out by both Carpenter et al. (1998)[6] and Vilholm et al. (2008).[7] Another factor that can explain higher frequency of pain in our study is due to the fact that women presented tumours that were in a more advanced stage (higher or equal to IIB), in 44.6% of all cases. On the other hand, Carpenter et al. (1998)[6] observed that 90% of patients presented smaller or equal staging to IIB. Vilholm et al. (2008)[7] did not evaluate disease staging.

Taking into account the characteristics of the population studied, the mean age of patients (58 years old) was compatible with the mean age of populations chosen in other studies.[8–11] We have observed bivariate analysis and we have confirmed, by means of logistic regression, that younger women show higher risks of developing pain syndrome. In other studies, a similar result has also been demonstrated.[4,8–12]

However, Montgomery and Bovbjerg (2004)[13] did not observe any association between age and acute pain in patients who underwent subdued surgical treatment for breast cancer. The difference which was assessed in this study can be related to the classification of the type of pain (acute vs. chronic), the assessment methodology (physical examination vs. interviews on telephone or by questionnaire), the type of study (prospective study vs. retrospective) and the type of operation. Kroman et al. (2000)[14] justified that younger women exhibit a higher risk for pain because their tumour tends to be more aggressive, associating their surgical treatment to chemotherapy and radiotherapy. Also, some patients can show higher emotional liability at the preoperative stage.[2] MacDonald et al. (2005)[4] stated that the relation between age and pain is not clear; they also proposed that women suffering from chronic pain can reduce physical activity and experience weight gain. In addition, young and obese women show risk factors independent of chronic pain when they are submitted to other types of operation, as for example, cardiac operation.

In terms of education, our population comprised of women from low schooling levels (46.6% illiterate or incomplete degree at primary school). In Katz et al. (2005)[10] 50% of all patients in the study had completed their studies. Carpenter et al. (1998)[6] observed that women's schooling lasted 13 years.

In relation to employment, 52.3% women presented instable welfare. Carpenter et al. (1998)[6] verified that 49% of all women in the study used to work all day long or part-time, but they have not defined any kind of employment bond. In our study, it was testified that 59.1% of women held housework as the main role; no other study has referred to this as the main activity of the patients, confirming, therefore, cultural differences among the population taken for the study.[7–11]

In relation to marital status, Smith et al. (1999)[9] and Poleshuck et al. (2006)[11] observed that 68.9% and 70.5% of women, respectively, were married; in our research, 52.3% women lived with a partner; none of the works presented this variable with statistical significance for the development of pain.

Despite the high prevalence of obesity in our population (72.3% of all women were classified as overweight or obese), this variable was not associated with pain occurrence, affirming the findings of MacDonald et al. (2005).[4] However, Smith et al. (1999),[9] verified that increased body mass index was a highly significant risk factor in pain occurrence.

In relation to psychological profile, 75.1% of all women presented altered mood (anxious, depressed mood or anguished) upon initial psychological assessment. However, such relation with pain was not statistically significant. Poleshuck et al. (2006)[11] could not observe significance between emotional alteration and risk of pain as well. However, Katz et al. (2005)[10] verified that some emotional aspects, such as anxiety, depression and hypochondria, have presented association with acute pain at bivariate analysis and only anxiety kept such position after multivariate analysis. Tasmuth et al. (1996)[15] described the correlation between chronic pain and levels of anxiety (preoperative), but the type of statistical analysis used in the study was not specified. However, these authors have all used validated and specific questionnaires to this means, as in our study these aspects had been sampled through the psychologist's handbook report.

When observing association between pain syndrome and the type of surgery, Tasmuth et al. (1997)[8] verified an increased number in radical surgeries, but it was verified that conservative surgeries had presented significantly higher risks to pain that was also observed by Carpenter et al. (1998).[6] Tasmuth et al. (1997)[8] justified that pain can be related to radiotherapy treatment, that is always applied after conservative surgeries. Carpenter et al. (1998)[6] related it to the highest relapse index that was found after the same treatment. In our study, despite the higher frequency of mastectomy (73.6%), there was no significant difference in pain occurrences reported across various types of surgeries. The findings were similar to that of MacDonald et al. (2005),[4] who compared two different types of mastectomies.

Radiotherapy may cause persistent pain in the breast cancer survivors.[16] Tasmuth et al. (1995)[17] stated that axillary involvement is related to pain and underlined the need to remove as much lymph nodes associated with radiotherapy adjuvant treatments over brachial plexus that was possible. Chemotherapy or hormone therapy, however, did not assess the relationship of the number of removed lymph nodes and the risk of pain. Poleshuck et al. (2006)[11] and Gartner et al. (2009)[12] observed, by means of a multivariable analysis, that women submitted to more radical surgeries demonstrate higher risks of removing lymph nodes during the surgery. Some studies[4,9,13] did not assess any association between pain and axillary approach. In our study, we have verified that the sentinel lymph node biopsy is a protection factor for the development of pain syndrome. After controlling the confounding and interaction variables of women submitted to axillary approach, we found that the removal of more than 15 lymph nodes has shown risks 2.01 times higher in relation to those who were submitted to less radical surgeries. No association between pain and adjuvant treatments was observed in our study.

Conclusion

The incidence of pain syndrome 6 months post-breast cancer surgical treatment was 52.9%. In relation to sensitive alteration, 52.6% patients have shown intercostobrachial pain, 1.3% neuroma and 3.2% have related phantom breast pain. Pain on the shoulder and/or thoracic-scapular area as a consequence of breast cancer surgical treatment was observed in 27.2% patients.

Younger women (<40 years) and those who were submitted to axillary lymphadenectomy (with more than 15 removed lymph nodes) have shown risk of developing pain syndrome after breast cancer surgical treatment.

Conflict of interest statement

The authors certify that there is no conflict of interest with any financial organisation regarding the material discussed in the article.

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