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Pain and Sensory Dysfunction after Breast Cancer Surgery: Neurometer CPT Evaluation

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Abstract. *The purpose of our study was to evaluate the presence of anatomical and functional damage to the afferent and sensorial fibres using the Neurometer CPT test. A questionnaire regarding pain was sent to 300 women who had undergone surgery six months earlier. Out of 300 patients 67 did not respond; 105 experienced no pain; while 128 felt pain. One hundred and twenty-eight women were divided into two groups: mastectomy with reconstruction and simple mastectomy. The intensity of pain at T0 in women with reconstruction was significantly higher; at T4, on the other hand, was lesser and there was no significant difference between the two groups. In both groups at T4, the daily diary revealed that interference with sleep and normal daily activities were more evident in patients who had undergone reconstruction ($p>0.001$). The final results at T4 demonstrated that among patients with reconstruction, 47% showed slight hypoesthesia-paraesthesia in the breast, armpit and arm zones, 39% slight hypoesthesia in the same locations and 18% severe hypoesthesia. Patients with reconstruction, instead, showed different percentages: 75% showed slight hypoesthesia-paraesthesia, 16% a slight hypoesthesia and 9% severe hypoesthesia. Our results support the utilization of the Neurometer CPT test as a device for monitoring post-mastectomy pain.*

Post-mastectomy pain is a frequent occurrence in patients who have undergone this type of surgery and it is estimated to occur in about 10-30% of the cases (1-4). Pain is manifested particularly during the 30-60 days following surgery, after the post-operative period is over. Patients experience heightened depression associated with the loss of an organ, which has both functional and esthetic implications. Post-mastectomy alterations in sensation and chronic pain are an area of breast cancer therapy that has not been extensively described. After the post-operative period and once the acute pain has subsided, the oncological-surgical team is inclined to treat the patient's painful symptoms as a temporary event. Pain persisting longer than 7-8 months could indicate that irreversible neurological damage has occurred during surgery. While the incidence of pain after surgery is high, its basic processes are not well known. Using conventional neuro-physiological methods, it is difficult to widely document this occurence, due to nerve damage and/or entrapment or compression near the area subjected to surgery, which is likely responsible for the spontaneous pain and alterations in normal somato-sensorial stimuli (5).

The goal of this study was to use the Neurometer CPT test to evaluate the presence of anatomical and functional damage to the afferent and sensorial fibres Aβ, Aδ and C (6) and to investigate the correlation between the type of surgical operation and the symptoms produced.

Materials and Methods

The clinical records of patients operated for breast cancer during the six months previous to this writing at the IX Unit of the General Surgery and Plastic Surgery Departments at the Second University of Naples, Naples, Italy. The records were studied to obtain data regarding the type of surgical operation, type of reconstruction (if any), presence or not of an implant, type and position of the implant, time of reconstruction (immediate or postponed), cancer therapy and presence of pain and paraesthesia at the time of the evaluation.

Among the women who were interviewed (Figure 1), 128 (43%) (median age 55±1.89 years) were included in our study. They were then divided into two groups according to the type of operation: mastectomy with reconstruction and simple mastectomy.

The exclusion criteria included: severe psychiatric and organic disorders; metastases; lymph edema; radio- or chemotherapy; rheumatoid and/or autoimmune arthritis; arthritis; Raynauld's disease; no pain or VAS ≤1.

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QUESTIONNAIRE

SURNAME AND NAME _____

AGE _____

- Do you feel pain after your breast surgery?
Yes/no

If your answer is no, you can stop here. If it is yes, please continue.

- When did pain appear?
1) immediately after the operation
2) after some weeks
3) after some months

- Where is the pain located?
1) in a specific area of your breast (write where)_____
2) all over breast and thorax
3) arm (write where)_____

- Is the pain continuous or intermittent?
Continuous/Intermittent

- If the pain is intermittent, does it last for long:
1) seconds
2) minutes
3) hours
4) days

- Did you suffer from depression?
Yes/No

- Did the worst pain appear when you were depressed?
Yes/No

- Is the pain related to all physical activity, such as moving or getting dressed?
Yes/No

Figure 1. *Questionnaire.*

The inclusion criteria included: women who underwent an unilateral breast cancer operation including removal of axillary lymph nodes without recurrences; reconstruction with immediate implants underlying the muscle (skin-sparing); no reconstruction; presence of sensorial and/or painful chest problems; diseases in the area of the incision, armpit, arm and ipsi-lateral hand; VAS ≥2. At the time of screening, following written informed consent, an accurate patient's history was gathered, followed by a clinical-neurological examination and by a McGill pain questionnaire to evaluate pain (short form) (7) and VAS. ECG was used to exclude possible connections between chest pain and cardiac pathology (8), and routine laboratory screening for indicators of inflammation (sedimentation rates, C-reaction protein, antistreptolysin) (9) were performed. The clinical-neurological examination was completed bilaterally and symmetrically by a consecutive evaluation of sensibility: tactile, superficial pain, deep tactile, vibratory and deep pain sensibility. The study of each patient lasted eight months. The sessions were conducted as follows:

First session (T0): six months after the operation.
Second session (T1): 30 days after the first session.
Third session (T2): 60 days after the second.
Fourth session (T3): 60 days after the third.
Fifth session (T4): 90 days after the fourth.

The electro-diagnostic exam using the Neurometer CPT test (Neuval Software) (10) was conducted by placing electrodes on the painful areas (referring to the clinical exam), and along the dermatometric distribution of the nervous fibers that had to be evaluated (Figure 2). A CPT measurement represents the minimal quantity of an electrical, neuro-selective, trans-cutaneous nonpainful stimulant required to evoke a sensation. Neuro-selectivity was obtained by the application of sinusoidal electrical stimulation of different frequencies. Each site was examined by the use of three different electro-stimulation frequencies: 2000, 250 and 5 Hz. In this manner, the stimulation of large and small myelinic fibers and amyelinic fibers was obtained. As such, three values independent of the CPT test were obtained and appropriately registered in the software database, stored and evaluated, based on the condition of the tested nerves.

In our study, the CPT exam was performed by positioning electrodes on the standard terminations and related algogenic areas, by delivering a current of 5, 250 and 2,000 Hz. We proceeded in an antidromic direction along the distribution pathways of the nervous structures. The electrodes were positioned on the following sites: the back of the hand, the forearm, arm, deltoid muscle, chest and breast (Figure 2). The threshold of perception to different electrical stimulations, calculated by a computerized system, allowed us to distinguish among the following conditions: no pain, slight or moderate discomfort and slight, moderate or severe hypoesthesia to complete anesthesia. During each visit, the patients underwent a clinical neurological examination, and completed the McGill pain questionnaire and CPT test. Their monthly diary was read for a daily evaluation of their pain, intake of the prescribed medicines (NSAIDs if necessary) and other aspects, such as interference with sleep and daily activities.

The student's *t*-test, at a confidence interval of 95%, was used to compare the values for pain intensity, average age, neurological examination and daily diary. The results of all tests were considered statistically significant at $p<0.05$. The χ^2-test was used to evaluate the association between the degree of pain documented with the Neurometer at time T4 and the type of plastic surgery performed.

The "null" hypothesis can be formulated, asserting that there is no association between the degree of pain documented with the Neurometer and the type of plastic surgery; the alternative hypothesis (Ha) is that there is an important link. The χ^2-test was used and the level of significance was set at $\alpha=0.05$ with gl=(r-l) (C-1) for a distribution χ^2 with gl=2, $p<0.01$. When $p<\alpha$, the "null" hypothesis was ruled out and it was concluded that there was a significant association between the presence of pain at T4 evaluated with the CPT test and the type of surgical operation. The tests were performed using the SPSS program (version 11.0) for Windows.

Results

Out of the 300 patients to whom the questionnaire was sent, 67 (22%) did not respond, 105 (35%) did not mention pain, while 128 (43%) spoke of pain. The age

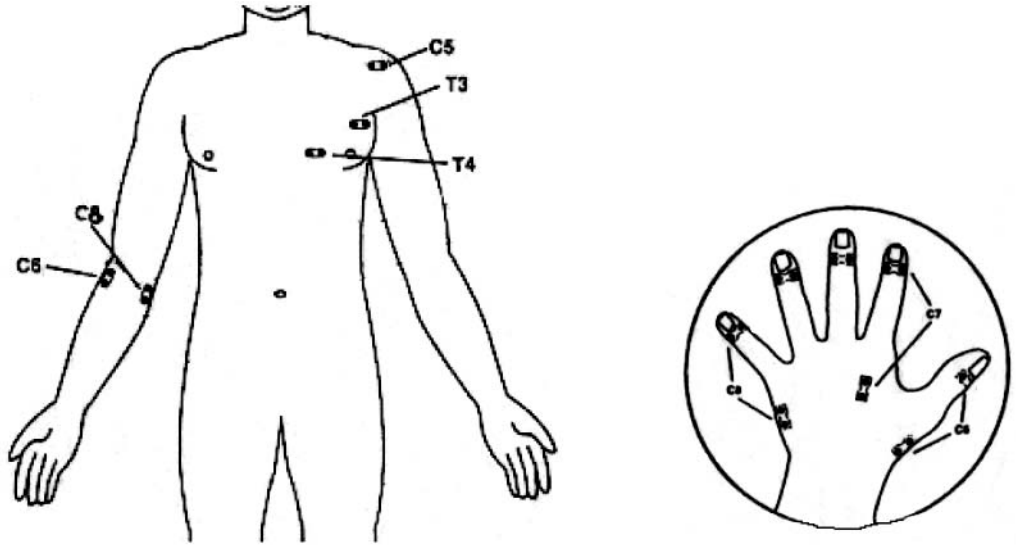

Figure 2. *Electrodes position along the dermatomeric distribution of the nervous fibers that had to be evaluated.*

(average±SD) of both groups is shown in Table I. The age of patients who accepted reconstruction was significantly lower ($p<0.0001$) than those without reconstruction.

Regarding the blood tests performed at T0, more than one of inflammation was highly evident in both groups, for all patients (Tables I, II, III).

The intensity of pain expressed using the VAS score was significantly higher at T0 ($p<0.0001$) in patients with reconstruction (5.26±1.33) compared to those who had undergone a simple mastectomy (4.27±1.9) (Figure 3).

Overlapping values, instead, were shown at T4 for both groups (VAS mastectomy and reconstruction = 2.66±1.33; VAS simple mastectomy = 2.53±1.01) and no significant difference was found ($p<0.53$) (Figure 4). In addition the patients with mastectomy and reconstruction did not show significant differences in their description of sensorial pain compared to patients who underwent mastectomy only (Table IV, Figure 5).

During the neurological examination at T0, patients in the group who had undergone mastectomy and reconstruction revealed the following: allodynia in the area near the wound (95%), negative pin-prick test in the breast area (87%), negative pin-prick test at the level of the homo-lateral upper limb (56%) and/or presence of alterations in vibratory perception in the breast area (75%).

Those patients with simple mastectomy, instead, revealed the following: allodynia in the area near the wound (85%), negative pin-prick test in the breast area (75%), negative pin-prick test at the level of the homo-lateral upper limb (46%) and/or presence of alterations in vibratory perception in the breast area (35%) (Table V).

Table I. *Median age of the patients of the two groups studied.*

	Mastectomy + reconstruction	Mastectomy	*P*-value
Age (years± SD)	48±2.21	62±1.58	$p<0.0001$

Table II. *Indicators of inflammation at time T0.*

	Mastectomy + reconstruction	Mastectomy
C-reaction protein	12 mg/L	11 mg/L
Sedimentation rates	32 mm/h	32 mm/L
Antistreptolysin	<330 U/mL	<330 U/mL
Leucocytes	$12.8x10^9$ L	$11.8x10^9$ L
Neutrophiles	$8x10^9$ cell/L	$7.9x10^9$ cell/L

Table III. *Indicators of inflammation at time T4.*

	Mastectomy + reconstruction	Mastectomy
C-reaction protein	9 mg/L	< 8 mg/L
Sedimentation rates	31 mm/h	< 30 mm/L
Antistreptolysin	< 330 U/mL	< 330 U/mL
Leucocytes	$11.8x10^9$ L	$10.8x10^9$ L
Neutrophiles	$7.8x10^9$ cell/L	$6.5x10^9$ cell/L

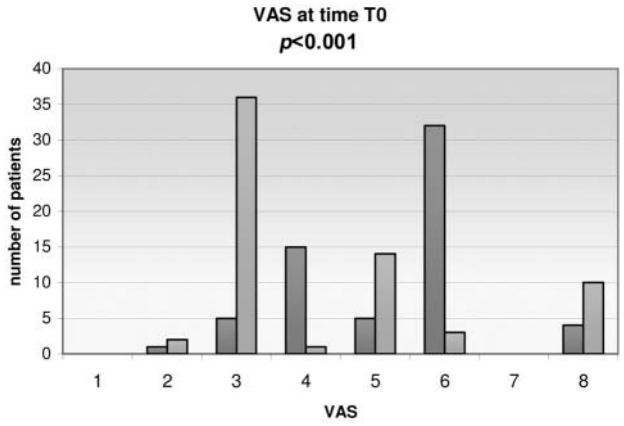

Figure 3. *Pain measurement at time T0.*

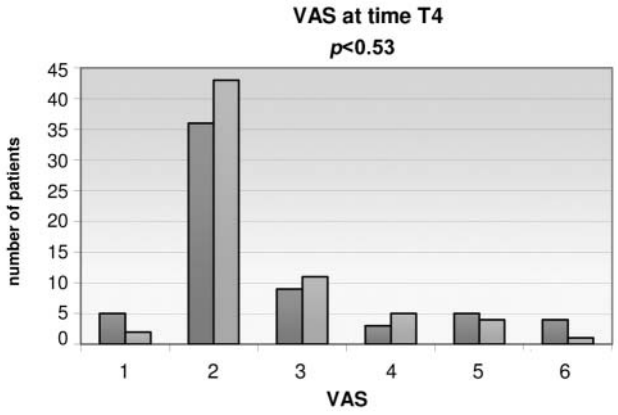

Figure 4. *Pain measurement at time T4.*

Table IV. *Distinctive features of pain.*

Description of pain	Mastectomy + reconstruction	Mastectomy
1. throbbing	3	8
2. like a spring, it goes off	0	0
3. it is like a stab	0	0
4. it is sharp like a razor-blade	0	0
5. gnawing	0	0
6. cramping	8	3
7. hot/burning	27	20
8. causes suffering	22	27
9. oppressive	18	15
10. sensitive to touch	5	10
11. splitting	7	8
12. tiring/exhausting	10	9
13. repulsive	0	0
14. alarming	0	0
15. vexes- it is cruel	0	0

Each number is the percentage of patients who gave a positive answer to the description of the type of pain.

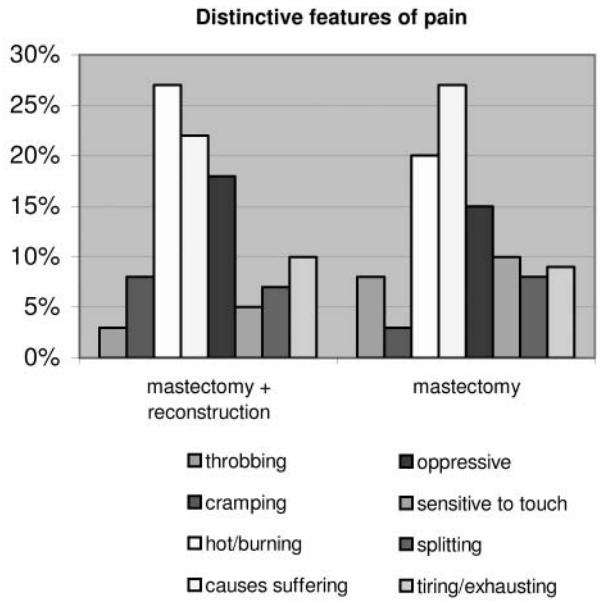

Figure 5. *Features of pain.*

The final results of the neurological examination at T4 in the mastectomy + reconstruction group showed: allodynia in the pericicatrizating area (85%), negative pin-prick test at the level of the homo-lateral upper limb (35%), negative pin-prick test in the breast area (67%) and/or presence of alterations in vibratory perception in the breast area (61%).

The same exam in the group of patients who had undergone a simple mastectomy revealed: allodiny in the pericicatrizating area (59%), negative pin-prick in breast (37%) unaltered pin-prick at the level of the upper homo-lateral limb (37%), and/or no alteration in vibratory perception in the breast area (68%) (Table VI).

The final results at time T4 with the Neurometer CPT test indicate that among patients with reconstruction, 47% had a slight hypoesthesia-paresthesia in the areas of the breast, armpit and homo-lateral limb, 35% a moderate hypoesthesia in the same anatomical regions and at least 18% had severe hypoesthesia. On the other hand, patients without reconstruction showed different results, at the same time and in the same anatomical regions: 75% noted slight hypoesthesia, 16% noted moderate hypoesthesia and 9% severe hypoesthesia (Table VII).

At time T0, the Neurometer showed a score of 9.54 and of 2.65 at T4 (a score of 0 was normal) ($p<0.01$) (Table VIII).

The results obtained from the daily diary of both groups at T4 showed that interference with both sleep and normal

Table V. *Results of the clinical neurological examination at T0.*

	Mastectomy + reconstruction	Mastectomy	*P*-value
Presence ofallodynia in the cicatrix area	Yes (95%)	Yes (85%)	$p<0.23$
Pin-prick test in the breast area	Pin-prick negative (87%)	Pin-prick negative (75%)	$p<0.10$
Pin-prick homo-lateral upper limb	Pin-prick negative (56%)	Unaltered (46%)	
Presence of alterations in vibratory perception in breast area	Yes (75%)	No (35%)	$p<0.10$

Table VI. *Final results of the clinical neurological examination at T4.*

	Mastectomy + reconstruction	Mastectomy	*P*-value
Presence of allodynia in the cicatrix area	Yes (85%)	Yes (59%)	$p<0.001$
Pin-prick test in the breast area	Pin-prick negative (67%)	Pin-prick negative (37%)	$p<0.001$
Pin-prick homo-lateral upper limb	Pin-prick negative (35%)	Unaltered (65%)	
Presence of alterations in vibratory perception in breast area	Yes (61%)	No (68%)	$p<0.001$

Table VII. *Final results of the Neurometer CPT test at T4 (breast area, armpit and homo-lateral limb).*

	Slight hypoesthesia	Moderate hypoesthesia	Severe hypoesthesia	Total
Mastectomy + reconstruction	29	22	11	62
Mastectomy	50	10	6	66
Total	79	32	17	128

χ^2-test $p<0.01$

Table VIII. *Sensitivity.*

Nerves that returned to normal function	3 (33.4%)	5 (55.7%)	$p<0.01$
Better nerves	1 (11.1%)	2 (22.1%)	$p<0.01$
Worse nerves	3 (33.4%)	1 (11.1%)	$p<0.05$
Stationary nerves	2 (22.1%)	1 (11.1%)	$p<0.05$
Total of studied nerves	9 (100%)	9 (100%)	

Table IX. *Final results of the daily diary at T4.*

	Mastectomy + reconstruction	Mastectomy	*P*-value
Interference with sleep	Yes (↓↓)	No	$p<0.001$
Pain	Slight	Slight	
Interference with daily activities	Yes (↓↓)	No	$p<0.001$

daily activities was more relevant in patients with mastectomy with reconstruction than in those with simple mastectomy. A significant difference was shown ($p<0.001$) (Table IX).

Discussion

Several theories regarding the mechanisms of sensorial disease and pain after a trauma can be applied to our study.

The whole innervation of the breast in association with the brachial plexus is anatomically complex. The nerves running through the deep musculature of the thoracic wall include the long thoracic, dorsal thoracic, lateral pectoral, and the median pectoral nerve. These nerves are usually unbridled during a mastectomy and can be traumatized (11). Also, the manipulation of the skin, which is richly innervated, can be the cause of pain along the cicatrix (12).

At the beginning of our study, we predicted that pain following reconstruction and dysesthesia after six months would disappear spontaneously. Our study, however, demonstrates that pain regressed while sensorial dysfunction remained, as confirmed by the CPT test at T4. There are some possible explanations for this result. The higher incidence of this kind of problem in the group of reconstructed patients could be due to a wider surgical dissection made to better insert the implant. Focal traumas can cause short interruptions in demyelinization that generate primary and secondary activity with a rise in axonal sprout (13). The scarring and chronic compression, with subsequent ischemia, can cause alterations in large and small myelinic fibers (14). The lateral and median pectoral nerve and the long thoracic nerve derive from the brachial plexus and extend under the large pectoral muscle. In the implants, beneath the muscle, the formation of a capsule that is not reactive can cause a compression. We are inclined to reject

this hypothesis, since the signs of phlogosis at the time the blood tests were performed were not statistically significant.

The common sign of significant hypoesthesia revealed by the Neurometer confirms a mechanical compressive effect in patients with reconstruction.

The CPT is used for two types of analysis including an analysis of the range of the neuropathy, from hyperesthesia to hypoesthesia, to compare the values of the area tested with normal values at 2,000Hz, 250Hz and 5Hz as well as an analysis of the ratio calculated to evaluate the values obtained for each frequency. The two types of ratio analysis available with CPT are either: a) between sites, comparing the ratio with counterlateral sites, or b) within the same site, comparing the different frequencies obtained from the CPT itself.

The evaluation of the ratio indicated a sensory dysfunction on the first stage, while analysis of the range showed the functional damage. Low values of the CPT test indicate an alteration in nervous function (hyperesthesia), while high values denote the loss of nervous function (hypoesthesia).

The threshold of perception of different electrical stimuli, analyzed by a computerized system, allowed us to observe the following: no anomalies; slight or moderate sensory dysfunction, slight or moderate hyperesthesia; slight, moderate or serious hypoesthesia, up to complete anesthesia. The McGill pain questionnaire was used to record any peculiarities in the patients' pain. It is well known that high anxiety levels and other emotional factors can affect the value of the questionnaire.

There was no significant difference found between the two groups in our study, probably because the breast reconstruction reduced the anxiety and depression normally caused by post-surgical impairment. Reconstruction was reported to improve the patient's emotional state, self image and sex life (15).

Conclusion

Our results suggest the use of the CPT Neurometer test as a valid electro-diagnostic exam in patients suffering from post-mastectomy pain. This procedure is not painful and is economically favorable. Our goal is to continue to expand our study to the screening of a large group of women and to longitudinal evaluations during clinical trials.

We are convinced that algological studies, following oncological and surgical treatment, could be a third component in the multi-modal therapy of breast cancer. Such studies could be extremely useful in identifying relevant problems connected with this pathology and, therefore, ultimately in improving therapy.

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