

Chronic Post-mastectomy Pain

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SUMMARY

Background. Surgery results in chronic pain in 7–80 percent of cases. One of the most frequently studied of these is chronic post-mastectomy pain. The prevalence was 40–50 percent in studies performed abroad. As this problem has not yet been studied in the Czech Republic, a retrospective prevalence study was performed to assess the extent of the problem and risk factors for development of chronic post mastectomy pain.

Methods and Results. An anonymous questionnaire was developed and distributed in various oncology departments and patients' organizations after ethical committee approval. The response rate was 100 percent; 330 questionnaires were processed. Chronic post-mastectomy pain (lasting longer than 3 months after surgery) was described by 69 (20.9 percent) women. The pain was permanent in 17 cases and transient in 46 cases, not specified in 6 cases. The pain intensity on the Lickert verbal scale was predominantly mild or moderate. Risk factors for development of chronic post-mastectomy pain were younger age (under 55–60 years, $p=0.0098$), less extensive surgery (tumourectomy vs. mastectomy, $p=0.0017$), intensive postoperative pain ($p=0.0002$) and radiotherapy ($p=0.0174$). A trend of chronic pain occurrence during chemotherapy ($p=0.0778$) was observed.

Conclusions. The prevalence of chronic post-mastectomy pain was lower in our study comparing to studies in other countries. The reason remains obscure despite detailed analysis.

Key words: breast cancer, surgery, chronic pain.

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There is growing evidence of a significant number of patients suffering from chronic pain after successful surgery due to progressive orientation not only to therapy result but also to subsequent quality of life (1). Breast cancer is the most frequent malignant disease in women in the Czech Republic, Europe and USA (source: www.uzis.cz). The majority of patients undergo surgical treatment. It was originally assumed that chronic post-mastectomy pain is rare. But with the enhancement of epidemiology, studies have been published indicating that a large number of women suffer from chronic pain, phantom pain and clysaesthesias. Chronic pain may result in psychic stress and limit normal daily activities. The most common prevalence of post-mastectomy pain described by different authors was between 40–50 percent of all operated patients (2). Pain can start any time after surgery and can persist longer than the time usually required for healing, i.e. minimally 3 months after surgery. The cause pain is not fully clear. In most cases, injury of nerves are considered. The characteristic of the pain is described in most cases as burning or lacinating, or it is compared to an electric current. Despite increasing interest in this issue, this problem has not been studied in the Czech Republic yet. As with other causes of chronic pain, it is not possible to accept unquestioningly results from countries with different cultural and social and economic backgrounds. Therefore we performed the present study. The aim of the study was, according to the recommenda-

tion of Crombie et al. (3), not only to find the prevalence of this phenomenon but also to find risk factors for development and moreover to obtain a view of necessity, application and quality of pain therapy.

METHODS

An anonymous questionnaire that resulted from revision of already published studies was developed after ethic committee approval, and it was divided into several parts. The consent of patient to participation in the study was the first item. The questionnaire further included basic demographic data and the type of surgery (total mastectomy, partial mastectomy, tumourectomy, extirpation of axillar lymph nodes) in the general section, and subsequent oncologic therapy (chemotherapy, radiotherapy). The next part concerned the history of intensive postoperative pain, presence of chronic pain (i.e. pain lasting longer than 3 months after surgery), its location, duration (permanent vs. transient and its duration), character (according to an abbreviated Czech version of McGill's Pain Questionnaire (4)) and intensity (mild, moderate, strong, severe). The last part concerned use of analgesics and their efficiency. The questionnaire was offered to patients treated in various oncology departments and also via the Mamma Help! Association to

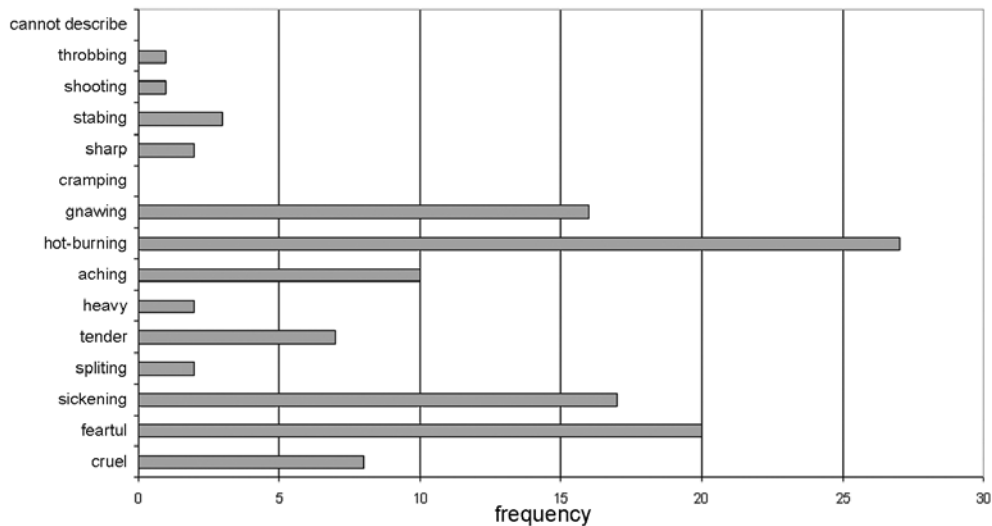


Figure 1. Pain characteristics

Tab. 1. Participating institutions

Institution	Number of respondents
University Hospital Královské Vinohrady, Prague	117
Masaryk Hospital Ústí nad Labem	104
Regional Hospital Pardubice	20
Hospital Havlíčkův Brod	4
Hospital Liberec	14
Patients' organisations	71

Tab. 2. Demography

Characteristics	Mean	Standard deviation
age	62.6	10.4
weight (kg)	73.2	13.6
height (cm)	164.0	8.1
Body Mass Index	27.4	7.5

Tab. 3. Pain intensity

Pain intensity	Number of respondents
without pain	261
mild	18
moderate	27
intensive	6
severe, unbearable	1
mild and moderate	6
moderate to intensive	7
changing from mild to severe according to the type and location	4

Note: Some respondents gave more answers (last 3 lines).

Tab. 4. Pain location

Location	Number of respondents
breast and/or scar	35
armpit and arm	15
both	16
no answer	3

women after breast surgery participating in various patients' organisations (Tab. 1). Every respondent had the chance to fill an anonymous questionnaire unattended checked by the staff (in the case of oncology department) after instructions about the voluntary nature of the exercise, and the questionnaires, filled in or blank (if a respondent choose not to participate) were placed in a sealed box. In addition to pain occurrence and its detailed description (see results), we also focused on detection or confirmation of some potential predictors of BOP factors published by other authors: age, Body Mass Index (BMI), type of surgery, subjective feeling of depression, radiation therapy, chemotherapy.

Data were statistically evaluated using statistic software BMDP (5). Paired t-test was used for statistical comparison of mean age and BMI with other studies. Chi-square test (or Fischer's exact test) in contingency tables was also used for test of predictor factors. Value $p < 0.05$ was considered as statistically significant.

RESULTS

All 330 distributed questionnaires returned completed; the response rate was 100 percent. A demographic characteristics of the sample is shown in Table 2. Most respondents (225) underwent total mastectomy, 40 respondents underwent quadrantectomy or partial mastectomy, 57 underwent tumourectomy and 8 did not give the type of surgery. Axillary dissection was performed in all respondents. Chemotherapy was recorded in 185 and radiotherapy in 271 questionnaires. Chronic pain in connection with surgery occurred in 69 (20.9 percent) respondents. Localisation and pain intensity are shown in Tables 3 and 4. Pain was permanent in 17 cases, transient in 46 cases and not specified in 6 questionnaires. Pain intensity on a four-point scale (mild, moderate, story, severe) was predominantly mild or moderate. Pain characteristics are shown in Figure 1. Pain was provoked or worsened by physical exercise but not by

Tab. 5. Number of respondents with pain according to the type of surgery

Type of operation	Number of respondents	Respondents without pain (%)	Respondents with pain (%)
total mastectomy	225	187 (83.1)	38 (16.9)
partial mastectomy	40	31 (77.5)	9 (2.5)
tumourectomy	57	35 (61.4)	22 (38.6)
not specified	8	8 (100)	0 (0)
total	330	261	69

feeling of depression (subjective respondent's evaluation). Only 37 percent of respondents with pain took some analgesics (in most cases non-steroidal anti-inflammatory drugs and tramadol) or physiotherapy; the administered therapy was sufficient for pain control in 69 percent of cases. Patients with intensive or severe pain were mostly treated with opioids and adjuvant therapy at the departments specialising in pain therapy.

Risk factors of chronic post-mastectomy pain were: younger age (under 55-60 years; $p=0.0098$), less extensive surgery (tumourectomy vs. mastectomy, $p=0.0017$) (Tab. 5), intensive post-operative pain ($p=0.0002$) a use of radiotherapy ($p=0.0174$). Trend in chronic pain occurrence during chemotherapy ($p=0.0778$) was observed.

DISCUSSION

The prevalence of chronic post-mastectomy pain was 20.9 percent in our study. These results are lower than in other studies. While we are aware that studies are incomparable from mathematical and statistic point of view, due to missing data or different criteria setting, we performed only imaginary statistical comparison. Differences are universally significant (Tab. 5). It is difficult to explain why the prevalence of chronic post-mastectomy pain in our study differs so significantly. There may be several possibilities.

Demography

Various authors (6-9) described an inverse relationship between the prevalence of chronic post-mastectomy pain and the age of respondents. The prevalence in the youngest group (30-49 years) was as high as 65 percent, and it decreased to 26 percent in group aged over 70 years. The prevalence of chronic post-mastectomy pain in our respondents older than 70 years was only 8.8 percent. Other authors either did not find any correlation between age and prevalence of chronic post-mastectomy pain or did not describe it.

The mean age of our respondents was 62.6 years, which is generally higher than in foreign studies. Nevertheless, the prevalence of post-mastectomy pain is lower in our study than the prevalence in even the oldest group in Smith's study (7). Another relationship described by the above authors is correlation between BMI and chronic pain. But mean BMI in our cohort was not so different from the Scottish population in Smith's study (27.4 vs. 26.2) to explain it and moreover, higher BMI was described as a risk factor (7).

Interval since surgery

Postmastectomy-pain does not change much with time, according to the literature (10, 11). Tasmuth et al. (12), who dealt with this factor, found the highest prevalence of pain immediately after surgery; only pain in the arm decreased between the sixth and twelfth month after surgery. The prevalence in other localisations did not change. Most other foreign studies were performed 6 to 10 months after surgery, which is similar to our sample.

Design of the study

Our questionnaire was developed after precise revision of adaptation of published studies. The only factors missing in our questionnaire were inquiries about loss of sensitivity and presence of lymphoedema – which presents a different problem from chronic pain. This item is also missing in some studies. Moreover, there was a place for description of other problems in our questionnaire, and one patient mentioned painless arm lymphoedema indeed. In this respect we used standard methods, which should not influence results.

Methodology

We distributed the questionnaire in various towns and institutions (capital city, regional capital and district capital, patients' organisations) to avoid bias. The result was not influenced by the site of collection. The extent of our sample represents more than 5 percent of the population which undergoes surgical treatment of breast cancer every year.

Surgical technique

Tab. 6. Theoretical comparison of our results with other studies

Paper	Prevalence in % (significance)	Number of respondents	Notes
Wallace, M. et al., 1996	31 ($p<0.001$)	<282	mastectomy only
Tasmuth, T et al., 1995	50 ($p<0.001$)	467	medium age 57-61 let
Kroner, K. et al., 1992	35,4 ($p<0.01$)	120	medium age 54
Hack, T. F. et al., 1999	31,1 ($p<0.01$)	222	mean age 57.1, SD 11.7
Tasmuth, T. et al., 1997	>39, or >22	293	various type and not localisation of surgery
Stevens, P. E. et al., 1994	20 NS	95	mean age 52
Borneth, S. et al., 2003	>50 ($p<0.001$)	180	mean age 55.3, SD 8.78
Amichetti, M. et al., 2003	43,8 ($p<0.001$)	324	medium age 59
Caffo, O. et al., 2003	39,7 ($p<0.001$)	570	medium age 60
Smith, W. C. S. et al., 1999	43 (83 including additional pain) ($p<0.001$)	408	65% prevalence <50 let, 26% prevalence >70 let
our results	20,9	330	

The cause of chronic post-mastectomy pain probably has multifactorial origin. Nerve injury is mostly hypothesised, especially during axillary dissection (7). Injury of intercosto-brachial nerve is likely to be responsible in particular for arm pain. All our respondents underwent axillary dissection, so we should detect a higher prevalence of chronic pain in comparison with existing studies – not a lower prevalence. Most authors, in accordance with our finding, found higher prevalence of pain after less extensive surgery; only Smith et al. (7) did not find any correlation between type of surgery and prevalence of chronic post-mastectomy pain. Admittedly, extensive surgery like Halsted surgery from the end of 19th century is not used at present, but the interval between our study and other studies is not so great that the progress in surgery could explain the difference.

Different cultural and social background of our population

Different pain perception in different populations is a permanent moot point. Nevertheless, after exclusion of the aforementioned factors, this explanation seems to be the most probable.

Pain characteristics are described especially by the terms designating sensory descriptors (4), which can be interpreted as a chronic pain with small mental super-structure. Two different groups can be seen in descriptions (Figure 1). The first one corresponds with the descriptors of neuropathic pain; the second group of terms describes more or less tissue damage. It matches already published extensive review (10). Our results are in accordance with previous studies, though their results are not always uniform. An example is the extent of surgical trauma. The majority of authors (6) in accordance with our findings described higher incidence of chronic post-mastectomy pain after conservative methods (partial mastectomy, mamma saving surgery); one paper (13) found the opposite result (radical mastectomy in comparison with less extensive surgery increases incidence of chronic pain) and other papers (12, 14) did not find any correlation, though positive correlation between number of extirpated axillary lymph nodes and post-mastectomy syndrome has been described (14). Even the influence of subsequent oncology therapy does not give definite results. Hack et al. (14) described that chemotherapy only and no radiotherapy is predictor of post-mastectomy pain. Tasmuth et al. (9) supposed that both radiotherapy and chemotherapy increases prevalence of post-mastectomy pain. This has not been confirmed by other authors who described only influence of radiotherapy (15) or no correlation at all (8, 11). Our results confirm the positive influence of radiotherapy ($p=0.0174$), with a similar trend for chemotherapy ($p=0.0778$). But use of both methods is influenced by other factors that are beyond of analysis from our questionnaire. There are not many studies concerning influence of acute post-operative pain on prevalence of chronic pain. But in spite of the fact that some of them did not confirm the correlation (16), others are in accordance with our results. There could be an additional possible cause of low prevalence of respondents' post-mastectomy pain; results of ongoing study concerning post-mastectomy pain (data has not been published yet) indicate that acute pain intensity after breast surgery is generally low.

CONCLUSION

To sum up, intensity of chronic post-mastectomy pain is lower in our population than in comparable foreign studies. The cause could be either generally different perception of pain in our population or better acute post-operative pain therapy. The predisposing factors of

chronic pain development after breast surgery are younger age, less extensive surgery, intensive post-operative pain, use of radiotherapy; a trend in chronic pain occurrence during chemotherapy was observed.

Abbreviations

BMDP – Bio Medical Data Package
BMI – Body Mass Index

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Commentary on paper by the authors Málek J. et al. “Chronic Post-mastectomy Pain”

Possible causes of low prevalence of chronic neuropathic pain after breast surgery detected in Czech women

The paper by Málek and colleagues focuses on an important subject – chronic postoperative pain originating after surgical and oncological treatment of breast cancer, the most common tumour disease in women. It is based on the results of a questionnaire project prepared according to accepted standards. The results from questionnaires sent to 330 women who underwent breast cancer surgery and were subsequently monitored at oncology or surgery departments in five Czech hospitals or in organizations for patients - all 330 of whom replied - are highly surprising and raise a lot of questions.

The authors mention some of them in their paper and try to respond. A 100 percent response rate for distributed questionnaires is very unusual. It compares with the usual 50 percent response rate, maximum, for questionnaires distributed to the patients suffering from various diseases. This fact alone, which suggests a high degree of co-operation and perhaps a positive motivation on the part of the patients, would deserve explanation and commentary of authors. It can be a manifestation of a “different” or unusually helpful attitude on the part of the patients questioned, or possibly it is a consequence of other factors characterising this group of 330 Czech women after mastectomy. This group – as authors of the paper repeatedly point out – significantly differs in evaluation of prevalence and post-operative pain intensity from data obtained in questionnaire studies performed in similar groups of women in other EU states or overseas.

Chronic pain originating after breast surgery is considered by most authors to be neuropathic pain. Both damage of nerves after irradiation and the neurotoxic effect of most cytostatic drugs (especially cisplatin) participate in the origin and development of neuropathic pain in addition to local mechanical influences and post-operative scarring, which lead to different kinds of extensive and serious damage of peripheral nerves, primarily sensitive. The psychic status of individuals suffering from chronic neuropathic or neuralgic pain caused by tumour disease or of toxic-metabolic or post-inflammatory origin is also important. These patients very often suffer from sub-depression or depression, which unquestionably has a psychogenic component. At the same time, disturbed interpersonal relationships and worsening of communication can also aggravate the patient’s condition. These patients are frequent visitors to oncology and neurology outpatients departments and also, over the last decade, to departments dealing with chronic pain treatment – and here somatized depression is also important. They are henceforth inadequately treated, and their treatment does not take advantage of available and efficient medicine (1).

Málek and colleagues refer to the surprising finding that chronic neuropathic pain is lacking in a large percentage of Czech women who underwent major surgery for tumours, in comparison with cohorts of women who underwent surgery for breast cancer in other EU countries. This begs one question: what percentage of women after mastectomy in the group questioned was on long-term sick leave or disability pension? Furthermore, it is also important to know how many women who underwent mastectomy for a tumour returned to their job without significant damage to their quality of life and without symptoms of somatogenic and sociogenic depression or deprivation which would distress them.

The authors paid also address attention to the administration of common analgesics and some anodyns. However, they cannot significantly reduce neuropathic pain except for a partial exception – tramadol. However, the data evaluating differences of the effects of particular medicaments are not given. These observations are missing, and in the discussion no reasons are mentioned why preparations commonly used at present were not administered. These drugs include neuromodulators, designated primarily for treatment of seizure diseases, are constantly used at a higher dosage for treatment of neuropathic pain caused by metabolic, post-inflammatory, neural or mechanical factors. Gabapentin, pregabalin and recently also topiramate are considered to be standard anti-neuralgic medicaments used for treatment of neuropathic pain in diabetic patients or neuropathic pain connected with administration of cytostatics. However, these drugs have not replaced tricyclic antidepressants – amitriptyline, imipramine, nortriptyline, dosulepin. Antidepressants with influence on serotonin metabolism and sometimes also on the noradrenaline metabolism – citalopram, fluoxetine and especially venlafaxine, which gathers increasing attention, have been used over the last decade for reducing neuropathic and neural pain.

Patients suffering from chronic back pain and from pain that follows both unsuccessful conservative and surgery treatment are suitable as a control group which could possibly confirm the validity of surprising hypothesis of better pain tolerance – both after breast tumour surgery or other tumour disease followed by neuropathic pain. It is necessary to point out that Bruce et al. did not demonstrate statistically significant differences in development of post-operative pain originating in patients who underwent various surgical procedures (2).

In any case, neurologists, neurosurgeons and algologists still more often meet a rapidly-increasing group of patients complaining that their health status and mainly various poorly tolerate pain are progressively getting worse after neuro-surgery or spinal or intervertebral plates spondylo-surgery whose indication is in most cases irritable deficiency root syndrome of compression origin (3). It seems that for determining expected development of “spine surgery failure” a similar proved relation (according to the data of IHIS@) is valid when significantly higher incidence and prevalence of vertebrogenic diseases was found in regions with higher unemployment and lower income. It is obvious that the number of patients complaining of chronic post-operative difficulties, which are finally considered to be a consequence

of wrong indication or unsuccessful surgery, is increasing, and that these patients are becoming chronic patients of pain centres or (either without or after surgery) applicants for disability pension. The risk of "surgery failure" or development of toxic-metabolic neuropathy after surgery or complex tumour therapy is not insignificant. Psychosocial or other risk psychosocial factors are not fully appreciated as possible contraindications for surgery. Anyway, these patients are sooner or later granted partial (primarily) and sometimes full disability pension because of severe back pain, though this is usually because of depression and poor quality of life caused by long-term sick-leave. Women working manually, doing unqualified jobs, in depressive personal situations or trying unsuccessfully to find a job and registered at an Employment Office are plentifully (and clearly disproportionably according to the experience of this reviewer) represented among this wide group of "vertebrogenic" patients. It is surprising that – apparently - a large number of similar candidates was not found in the group of women questioned, who underwent mastectomy; it cannot be ruled out that women who have undergone breast ablation due to proved malignant disease do not find themselves under such strong social and assessment pressure as women suffering from relapsing "banal" back pain caused by spinal surgery. The psychosomatic component is commonly acknowledged in this group of diseases, as a cause of economical-social motivations which could undermine the relatively high percentage of disability pensions awarded for chronic pain caused by vertebrogenic disease or "spinal surgery failure".

The surprising result could indeed originate in the method of selecting patients, in the composition of the group and in age-related social factors – which the authors partially mention in discussion.

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