

Incidence and risk factors of chronic postoperative pain after breast surgery

Meme cerrahisi sonrası görülen kronik postoperatif ağrı sıklığı ve risk etmenleri

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ABSTRACT

Objective: The primary aim of this study was to determine the incidence of chronic postoperative pain after the types of breast surgery. The secondary aim was to examine the factors associated with chronic postoperative pain.

Methods: The prospective study included 240 female patients. Data were collected on: visual analogue scale (VAS) pain scores in the Post Anesthesia Care Unit (PACU) at 1st month and at 3rd-6th months postoperatively; and age, BMI, preoperative pain, radiotherapy, chemotherapy, postoperative acute pain, length of hospital stay were the measures taken into account.

Results: Chronic postoperative pain was experienced by 39.2% of patients at 3rd month and 18.3% of patients at 6th month. Chronic pain was detected in 41.8% of patients who had severe acute postoperative pain. BMI, age, preoperative and severe acute postoperative pain, the type of surgery, the length of hospital stay, development of complications, chemotherapy and radiotherapy treatment have been shown to be the risk factors in chronic postoperative pain after breast surgery. The incidence of postmastectomy pain syndrome (PMPS) was 29.5% in mastectomy cases, and 64% in those having mastectomy and axillary dissection.

Conclusion: As they are considered as complication of surgery according to some authors, chronic postoperative pain and post-mastectomy pain syndrome are commonly discussed and studied clinical problems in recent years. More comprehensive studies about its etiology, risk factors and pathogenesis to prevent or treat the chronic postoperative pain and post-mastectomy pain syndrome are warranted as it both reduces life comfort and causes workforce loss following surgery.

Key words: Postoperative pain, breast surgery, chronic pain

ÖZ

Amaç: Bu çalışmanın birincil amacı, farklı tiplerde meme cerrahisi sonrası kronik postoperatif ağrı insidansını, ikincil amacı, kronik postoperatif ağrı ile ilişkili faktörleri araştırmaktır.

Yöntemler: Bu prospektif çalışma 240 kadın hasta ile yürütüldü. Hastaların postoperatif değerlendirilme ünitesinde (PACU), postoperatif 1., 3. ve 6. aylarda VAS ağrı skorları, yaş, BMI, preoperatif ağrı, radyoterapi, kemoterapi, postoperatif akut ağrı ve hastanede kalış süresi verileri toplandı.

Bulgular: Hastaların %39,2'si 3. ayda ve %18,3'ü ise postoperatif 6. ayda kronik postoperatif ağrı deneyimi yaşamıştır. Ciddi postoperatif ağrı çeken hastaların %41,8'inde kronik ağrı tespit edildi. BMI, yaş, preoperatif ve ciddi akut postoperatif ağrı, cerrahi tipi, hastanede kalış süresi, komplikasyon gelişmesi, kemoterapi ve radyoterapi tedavisi meme cerrahisi sonrasında kronik postoperatif ağrı gelişimi için risk faktörü olarak belirlendi. Mastektomi yapılan hastalarda postmastektomi ağrı sendromu (PMPS) %29,5 oranında görülürken, aksiller diseksiyonla birlikte mastektomi yapılanlarda bu oran %64 olarak saptandı.

Tartışma ve Sonuç: Kimi otörler tarafından cerrahinin bir komplikasyonu olarak görülen kronik postoperatif ağrı ve postmastektomi sendromu son yıllarda sıkça tartışılmış ve çalışılmış klinik sorunlardır. Her ikisi de operasyon sonrası yaşam konforunu azalttığından ve iş gücü kaybına neden olduğundan postoperatif ağrı ve postmastektomi ağrı sendromunun önlenmesi veya tedavisi için etiyoloji, risk faktörleri ve patogeneze ilişkin daha ayrıntılı çalışmaların yapılması gerekmektedir.

Anahtar kelimeler: Postoperatif ağrı, meme cerrahisi, kronik ağrı

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INTRODUCTION

Despite developments concerning pain pathophysiology and treatment and new medications and the use of complex drug administration systems, the studies performed in this area has shown that 30-75% of the patients suffer from moderate to severe postoperative pain. Following operations such as inguinal hernia repair, breast-thorax surgery, leg amputation and coronary artery bypass surgery, acute postoperative pain preceded chronic pain in 5-85% of the patients. As chronic pain may be severe in 2-10% of these patients, chronic postoperative pain represents a major, mostly undiagnosed clinical issue ^(1,2).

Many studies reported that development of chronic pain after breast surgery is the most common problem with an incidence of 25-60% depending on the definition of incidence, measurement and treatment methods ⁽³⁾.

After ruling out other causes of pain such as recurrent painful episodes, chronic postoperative pain is defined as having pain related to surgical site over 3 months following surgery ⁽³⁾. Chronic postoperative pain has a negative effect on the quality of life and creates important economic consequences for health system. Many pre-, intra- and postoperative risk factors for the development of chronic postoperative pain have been claimed to be young age, high BMI, preoperative and postoperative severe acute pain, radiotherapy, chemotherapy and axillary surgery ⁽⁴⁾.

Many studies have investigated the persistent pain, its incidence and risk factors following breast cancer surgery ⁽³⁻⁷⁾. It is hard to compare them as they are very heterogeneous. Different presurgical and postsurgical assessment methods have been used and follow-up courses have differed widely. Many of them have been retrospective studies. Literature reviews have revealed that incidence and risk factors of chronic pain were not investigated in patients who had non-cancer breast surgery and compared to those in cancer patients.

The primary aim of this prospective study is to determine the prevalence of chronic postoperative

pain and postmastectomy pain syndrome (PMPS) following tumor excision in breast, cancer or reconstructive breast surgeries which are commonly performed nowadays. The secondary aim is to state the characteristics and precipitating risk factors of chronic postoperative pain.

MATERIAL and METHODS

This prospective observational study was performed on 252 volunteered patients over 18 years old, who had had breast surgery during the calendar year of 2011, and provided with detailed information about the study before they gave their undersigned "Patient Consent Forms". The study protocol was approved by the local ethics committee (12.01.2011-10/03). Exited patients, patients with other metastatic malignancies and uncooperative cases were excluded from the study.

The patients filled in the questionnaire forms the day before surgery. Background data included age, weight and height (calculated to body mass index), severity, duration, and characteristics of preoperative pain of any type, number of previous operations (other than breast surgery).

The patients were informed about VAS (Visual Analogue Scale 0 = no pain, 10 = severe pain) as this scale was used in order to assess their perception of pain during postoperative period.

The patient records were reviewed in consideration of the type of surgery (breast tumor excision, modified radical mastectomy, mastectomy with axillary evacuation, lumpectomy and bilateral reduction mammoplasty), complications of surgery: wound infection or hematoma (no/yes) or seroma (no/yes), chemotherapy (no/yes) or radiotherapy (no/yes). All patients were routinely given intravenous paracetamol and tramadol treatment during their hospital stay.

First, 6th, 12th, 24th, 48th hour and 1st month- postoperative painful episodes were defined as acute postoperative pain, and pain felt at 3rd and 6th postoperative months pains as chronic pain. In the presence

of chronic pain, severity (VAS), characteristics, similarities to preoperative pain and presence of other complaints (edema, dullness, redness) were questioned over the phone. Pain score VAS > 3 was considered moderate to severe pain.

For statistical analysis, SPSS (Statistical Package for Social Sciences) for Windows 18.0 program was used. All data were summarized with tables and graphics, in addition to descriptive statistical methods (mean, standard deviation, minimum, maximum value), Spearman’s Correlation Test was chosen for the analysis of the relation between abnormally distributed variables. Correlation coefficient “r” was between -1 and +1. Given p value of <0.05, “r” value which approached to +1 represented positively strong and “r” value closer to -1 showed negatively strong correlation. As “r” value got closer to 0, it indicated presence of a weak relation. Mann-Whitney U test was used for intergroup comparisons of abnormally distributed parameters and determination of the group that caused the difference. In comparison of qualitative data, “chi-Square test” and “Fisher’s Exact Chi-Square test” were used. Findings were evaluated within 95% confidence interval and at a level of significance of p<0.05.

RESULTS

The study included 252 participants who had breast surgery. However, 12 cases were excluded due to loss of contact over the time and the study continued with 240 patients. Mean age (47.5±14.1 yrs), body weight (69.8±10.1 kg), height (160.1±5.6 cm), and body mass index (BMI) (27.2±3.6 kg/m²) were also calculated.

Among 240 participants chronic pain was detected in 39.2%, and 18.3% of the patients at postoperative 3rd, and 6th months respectively.

There was a significant correlation between chronic postoperative pain and demographic data including age and BMI. The mean age and BMI were higher in those having chronic postoperative pain than those without (p<0.05) (Table 1).

Table 1. The effects of demographic characteristics over chronic pain.

| | Chronic Pain | N | Mean ± SD | P |
|--------------------------|--------------|-----|------------|-------|
| Age (years) | Yes | 94 | 50.3 ±12.3 | 0.007 |
| | No | 146 | 45.8 ±14.9 | |
| BMI (kg/m ²) | Yes | 94 | 31.6 ± 8.6 | 0.006 |
| | No | 146 | 24.1 ± 6.5 | |

BMI, Body Mass Index

Preoperative pain was not detected in 117 (48.8%) of 240 cases and among them, 28 (23.9%) had chronic pain. Preoperative pain was reported in 123 cases (51.2%), 58 of whom had a VAS score smaller than 3, and 65 of whom had a VAS score greater than 3 points. Patients’ distributions based on the characteristics of preoperative pain were as follows: stinging (26%), throbbing (25.2%), stabbing (20.3%), burning (9.7%), and combination of these characteristics (18.7%). Chronic pain was detected in 65 cases (53.6%). Analysis showed statistically significant correlation between development of chronic pain and preoperative pain (p=0.009), however any statistically significant correlation between the pain characteristic and chronic postoperative pain was not detected (p=0.802).

The duration of pain was evaluated in 123 patients with preoperative pain. Preoperative chronic pain lasted for one, 1-3, and longer than 3 months in 55 (33/60), 69.2 (18/26), and 59.5 % (22/37) of the cases, respectively. Statistically significant, and a strong correlation was found between the chronic postoperative pain and preoperative pain and its duration (p<0.001).

Fifty (39.1%) among 128 cases who had had previous operations for various reasons experienced chronic postoperative pain, while 78 (60.9%) had no chronic pain. There was no statistically significant correlation between chronic postoperative pain and previous operations (p>0.05).

Chronic postoperative chronic was observed in 13.2% of the patients operated for breast mass, in 56.9% of the patients operated for breast cancer and

Table 2. The association between chronic pain and surgical procedure.

| Operation indication | N | Chronic pain | | P = 0.000 |
|-----------------------------|----|--------------|------------|-----------|
| | | No | Yes | |
| Breast mass excision | 27 | 22 (81.5%) | 5 (18.5%) | |
| BRM | 38 | 29 (76.3%) | 9 (23.7%) | |
| Segmental mastectomy | 44 | 31 (70.5%) | 13 (29.5%) | |
| Lumpectomy | 16 | 14 (87.5%) | 2 (12.5%) | |
| MRM | 18 | 8 (44.4%) | 10 (55.6%) | |
| Segmental mastectomy + ALND | 53 | 19 (35.8%) | 34 (64.2%) | |
| Lumpectomy + ALND | 21 | 8 (38%) | 13 (62%) | |
| MRM + ALND | 23 | 11 (47.8) | 12 (52.2) | |

MRM: Modified radical mastectomy, BRM: Bilateral reduction mammo-plasty, ALND: Axillary lymph node dissection

in 25% of the patients operated for macromasty. There was statistically significant and strong correlation between chronic pain and these operations for breast mass, cancer and macromasty ($p=0.000$).

The relation between the type of surgical procedures and chronic postoperative pain was strong and statistically significant ($p<0.001$) (Table 2).

Chronic pain was experienced by 94 (41.8%) of 225 patients with moderate- severe pain ($VAS>3$) during acute postoperative course. None of 15 patients (6.3%) with mild but acute postoperative pain ($VAS<3$) had chronic pain. It was detected that acute and severe postoperative pain statistically significantly increased the incidence of chronic postoperative pain ($p=0.001$) (Table 3).

Chronic postoperative pain occurred in patients who stayed in the hospital after the operation for 36 ($n=11/58$; 19%), 48 ($n=60/137$; 43.8%), and 72 ($n=23/45$; 51.1%) hours. Incidence of chronic pain increased in parallel with longevity of the hospital stay ($p=0.001$) (Table 3).

Chronic postoperative pain was experienced by 65.2% of the patients who had radiotherapy and 64% of those who had chemotherapy and significant correlation was detected between the chronic pain and radiotherapy and chemotherapy ($p=0.009$) (Table 3).

Forty-three cases (17.9%) at postoperative 3rd month and 19 cases (7.9%) at 6th month had complications. Hundred percent of those having complications had chronic pain ($p=0.000$) (Table 3).

Table 2. Pre- and postoperative factors and their relationships with postoperative chronic pain.

| Risk factors | N | Chronic pain | | p |
|-----------------------------|-----|--------------|-------------|------------------|
| | | No | Yes | |
| Preoperative pain | | | | |
| Yes | 123 | 65 (53.6%) | 58 (46.4%) | 0.009 |
| No | 117 | 28 (23.9%) | 89 (76.1%) | > 0.05 |
| Previous operations | | | | |
| Yes | 128 | 50 (39.1%) | 78 (60.9%) | 0.001 |
| No | 112 | 44 (39.3%) | 68 (60.7%) | 0.009 |
| PACU acute pain | | | | |
| VAS > 3 | 225 | 94 (41.8%) | 131 (58.2%) | 0.000 |
| VAS < 3 | 15 | 0 | 15 (100%) | |
| Hospital stay length | | | | |
| Up to 36 hours | 58 | 11 (19%) | 47 (81%) | |
| 48 hours | 137 | 60 (43.8%) | 77 (56.2%) | |
| over 72 hours | 45 | 23 (51.1%) | 22 (48.9%) | |
| Radiotherapy | | | | |
| Yes | 23 | 15 (65.2%) | 8 (34.8%) | |
| No | 217 | 81 (37.3%) | 136 (62.7%) | |
| Chemotherapy | | | | |
| Yes | 25 | 16 (64%) | 9 (36%) | |
| No | 215 | 78 (36.3%) | 137 (63.7%) | |
| Postop Complication | | | | |
| 3rd month | | | | |
| Yes | 43 | 43 (100%) | 0 | |
| No | 197 | 51 (25.9%) | 146 (74.1%) | |
| 6th month | | | | |
| Yes | 19 | 19 (100%) | 0 | |
| No | 221 | 75 (33.9%) | 146 (66.1%) | |

N: patient number, VAS: Visual Analog Scale

The incidence of postmastectomy pain syndrome (PMPS) was 29.5% in mastectomy cases, and 64% in those having mastectomy and axillary dissection. Similarly, PMPS rate was 12.5% in the patients with lumpectomy and 61.1% in those having lumpectomy and axillary dissection.

In PMPS cases, the pain was on breast and axillary region at the operated side, and edema was also observed in arm, forearm and hand at the operated side.

At postoperative 3rd month, 94 patients (39.2%), pain felt mostly stinging (37.2%) and stinging and burning (27.6%), and less frequently throbbing, stabbing pain, and combination of these (Table 4). In terms of pain localization, 37 cases (39.4%) had the pain in breast, 22 (23.4%) in axilla and 35 (37.2%) in both breast and axilla.

At postoperative 6th month, 44 patients (18.3), most frequently felt stinging (50%), and both stinging and burning (20.5%) and less frequently burning,

Table 4. Pain characteristics in PMPS patients at 3rd and 6th months

| Postoperative 3 rd month N = 94 | | Postoperative 6 th month N = 44 | |
|---|------------|---|-----------|
| Burning | 7 (7.4%) | Burning | 4 (9.1%) |
| Stinging | 35 (37.2%) | Stinging | 22 (50%) |
| Throbbing | 5 (5.3%) | Throbbing | 3 (6.8%) |
| Stabbing | 5 (5.3%) | Stabbing | 2 (4.5%) |
| Stinging + Burning | 26 (27.6%) | Stinging + Burning | 9 (20.5%) |
| Stinging + Stabbing | 7 (7.4%) | Stinging + Stabbing | 3 (6.8%) |
| Stinging + Throbbing | 3 (3.1%) | Other | 1 (2.3%) |
| Throbbing + Stabbing | 5 (5.3%) | | |
| Throbbing + Burning | 1 (1%) | | |

throbbing, stabbing pain and their combination (Table 4). As for pain localizations, 14 cases (31.9%) had the pain in breast, 13 (29.5%) in axilla, and 17 (38.6%) in both breast and axilla.

DISCUSSION

According to our study’s findings, the incidence of chronic pain following cancer or non-cancer breast surgery was found to be 39.2% at postoperative 3rd month, and 18.3% at 6th month. PMPS developed in 35% of those who had mastectomy due to breast cancer. Previous studies about this topic reported incidence rates of 13-43% in breast cancer patients within the first year or later on following mastectomy (8-10). Although surgical techniques have been improved since the preliminary studies, a more recent study has showed clinically significant incidence (48%) of pain following partial or complete mastectomies (11). Legeby et al. (12) reported that 25 women complained of chronic pain 3-4 years after complete mastectomy with immediate reconstruction. Another study found very low incidence of chronic pain as 8.2% following breast surgery. Investigators reported that this low incidence of chronic postoperative pain might be related to patients not being included in study, those who had simultaneous axillary lymph node dissection which is known as a risk factor for chronic pain (13).

Secondary aim of this study was to detect the association between postoperative pain levels following breast surgery and various demographic data and clinical features. It is claimed that increased age reduces the risk of chronic postoperative pain in

breast surgery patients and postoperative pain is more severe and longer in young patients due to the possibility of the presence of bigger tumors (10) Smith et al. (10) reported incidence rates of chronic pain following mastectomy, as 26,40, and 65% in patients over 70 years, and those aged between 50-69, and 30-49 years, respectively.

We found a significant correlation between chronic postoperative pain and age (p<0.05). However, this relation appeared to be a linear correlation (for postop 3rd month r=+0,153, for postop 6th month r=+0,129). We noticed an increase in chronic pain with aging of the patients. In a study supporting this finding, Sipila et al. (4) noted that incidence of chronic pain increases in patients with breast cancer surgery with aging. As a reason for our assumption, it might be considered that we included not only the breast cancer patients but also those with other diagnoses such as breast mass and macromasty.

Positive correlation between chronic postoperative pain and high BMI was mentioned in many previous retrospective studies (10,13). Karki et al. (14) found, in their prospective study, that high BMI is associated with neck and shoulder pain at 6th and 12th months after breast cancer surgery. Moreover, it should be taken into consideration that obesity makes the practice of surgery more complicated. As a result of the study by Sipila et al. (4) the authors mentioned an increase in chronic postoperative pain as body mass index increases, similar to our study.

Many studies about hernia repair have showed that preoperative pain is a risk factor for chronic pain (15,16). Page et al. (15) found the pain scores of patients who had hernia operation, without preoperative resting pain, significantly low at postoperative 1 year. Nikolajsen et al. (16) noticed that risk of stump and fantom pain increases at postoperative early phase and at 3rd month in patients who had preamputation pain. However the relation between chronic pain after breast surgery and presence of preoperative pain in breast is controversial. While Poleshuck et al. (11) did not find any relation, Sipila et al. (4) noted preoperative pain as a risk factor. They associated this

discrepancy to the differences in study designs. We found significant correlation between preoperative pain and chronic postoperative pain ($p=0.000$). Besides, we also detected that duration of preoperative pain is also a determinant in the development of chronic postoperative pain following breast surgery as a risk factor not found in literature.

It was supposed that previously performed various operations may be a risk factor for chronic pain leading to sensitization of central nervous system. Sipila et al. ⁽⁴⁾ reported that requirements for previous operations might increase susceptibility to chronic pain and sensitization of pain pathways since these needs emerge due to chronic diseases and systemic inflammations. In this study, chronic pain developed more frequently following breast surgery in those who had had different operations previously without any statistically significant intergroup difference. We believe that it might be related to diverse patient populations being operated for cancer or non-cancer indications.

Many studies have shown associations between acute, and chronic postoperative pain ⁽¹¹⁻¹⁷⁾. In our study, presence of chronic pain in 41.8% of the patients with moderate-severe pain ($VAS>3$) during postoperative acute phase and lack of chronic pain in patients with mild acute pain ($VAS<3$) support the literature findings.

There are also publications claiming that treatment methods additional to surgery including radiotherapy and chemotherapy may increase the risk of chronic pain ^(6,11). In our study, we also found significant correlation between the incidence of chronic postoperative pain and radiotherapy and chemotherapy ($p=0.041$ and $p=0.021$).

In our study, we found a correlation between postoperative complications and chronic pain, which is similar to the results of the study by Ahmed et al. ⁽¹⁸⁾ we observed complications at postoperative 3rd, and 6th months in 17.9%, and 7.9% of the patients, respectively; however Ahmed et al. reported that a total of 13 patients (17.8%) had complications (wound infection, hematoma, seroma) during postoperative period

which played an effective role in the development of chronic pain ⁽¹⁸⁾. We also observed chronic pain in all patients with complications ($p=0.000$).

Post-mastectomy pain syndrome (PMPS) is a chronic postoperative pain type characterized with neuropathic pain, accompanied with symptoms such as burning, stinging or stabbing pain, edema, paresthesia and muscle weakness involving operation area or in ipsilateral arm following breast cancer surgery ⁽¹⁹⁾. The incidence of PMPS has been reported to be nearly 20-68 percent ^(19,20-22). Supportingly, we also found incidence of PMPS as 35 percent.

PMPS may occur right after surgical procedure or months later and stay for years. While it is not certainly known, it is believed that this clinical picture occurs after damage to intercostobrachial and intercostal nerves during mastectomy, lumpectomy and axillary dissection ⁽²³⁻²⁵⁾. The sensitivity to pain in PMPS is detected in anterior thorax, axilla and upper medial arm where the damaged nerves distributed ^(20,23,26). In our study, the locations of pain in csw PMPS were breast and axilla at the operation side and edema was seen in arm, forearm and hands at operation side. When axillary dissection is performed in the same session with mastectomy and lumpectomy, 80-100% of local nerves are injured ^(20,23,26). Hence, incidence of PMPS in patients who had undergone mastectomy, mastectomy plus axillary dissection, lumpectomy, and lumpectomy plus axillary dissection were 29.5, 64, 12.5, and 61.1%, respectively. The effect of axillary dissection over development of PMPS was found to be statistically significant ($p<0.001$).

As a feature that makes our study unique, we found that cancer surgery is a statistically important risk factor for the development of chronic postoperative pain ($p<0.001$) in comparison to non-cancer surgery.

The result of our study was limited by the following factors. As the center wherein this study was performed is a teaching hospital, the surgical team was not always the same which might be considered as a methodological limitation. Neuropathic pain

scales such as DN4 or LANSS were not used in this study to determine the incidence of neuropathic pain during the postoperative period. Besides the effects of psychological, social and/or economic factors effective on postoperative pain and also the short duration of study were not excluded .

As they are considered a complication of surgery according to some authors, chronic postoperative pain and post-mastectomy pain syndrome are commonly discussed and studied clinical problems in recent years. More comprehensive studies about its etiology, risk factors and pathogenesis so as to prevent or treat the chronic postoperative pain and post-mastectomy pain syndrome are warranted as they both reduce life comfort and cause workforce loss following surgery.

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