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# Post-Thoracotomy Pain Syndrome: Incidence, Neuropathic Component, and Risk Factors

## Post-Torakotomi Ağrı Sendromu: İnsidans, Nöropatik Bileşen ve Risk Faktörleri

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**ABSTRACT**

**Objective:** Pain that recurs or persists at least two months after thoracotomy is defined as post-thoracotomy pain syndrome (PTPS), and neuropathic pain (NP) is expected to develop in approximately half of these patients. This study aimed to examine the frequency of PTPS, the neuropathic component of pain, and the effecting risk factors in patients who underwent thoracotomy.

**Methods:** 862 patients who underwent thoracotomy were monitored between January 2010 and May 2013 at Gazi University Faculty of Medicine Hospital. The study continued with 277 patients who could be contacted by phone at least three months after the operation. In these patients, the presence of pain was questioned, if present, the severity of pain, NP and affecting risk factors were investigated. The pain severity and NP component were evaluated using the Numeric Rating Scale (NRS) and Douleur Neuropathique 4 (DN4) questionnaires, respectively.

**Results:** Severe PTPS frequency after thoracotomy was found to be 19.1 % and NP was present in 53% of patients with NRS 3-10. As the severity of pain increased, the frequency of NP and analgesic drug consumption increased ($p<0.05$). As risk factors gender, age, operation duration and epidural analgesia application did not significantly affect the frequency and severity of PTPS and NP. As the time after the operation increased; PTSP frequency, neuropathic pain frequency and pain intensity were decreased ($p<0.05$).

**Conclusion:** Severe PTPS is detected in approximately one in five patients who undergone thoracotomy and half of them had NP. The neuropathic component of pain increases as pain intensity increases and decreases as time passes after surgery. The development of PTPS and NP should be reduced by providing effective analgesia.

**Keywords:** Thoracotomy, chronic pain, post-thoracotomy pain syndrome, neuropathic pain

**ÖZ**

**Amaç:** Torakotomiden en az iki ay sonra tekrarlayan veya devam eden ağrı "Post-Torakotomi Ağrı Sendromu (PTAS)" olarak tanımlanır ve bu hastaların yaklaşık yarısında nöropatik ağrı (NP) gelişmesi beklenir. Bu çalışmada torakotomi ile operasyon geçirmiş hastalarda PTAS sıklığı, ağrının nöropatik bileşeni ve etkileyen risk faktörlerinin incelenmesi amaçlanmıştır.

**Yöntem:** Ocak 2010-Mayıs 2013 tarihleri arasında Gazi Üniversitesi Tıp Fakültesi Hastanesi'nde torakotomi uygulanan 862 hasta çalışmaya alındı. Çalışma, operasyondan en az üç ay sonra telefonla ulaşılabilen 277 hastayla devam etti. Bu hastalarda ağrının varlığı sorgulandı, varsa ağrının şiddeti, NP ve etkileyen raisk faktörleri araştırıldı. Ağrı şiddeti ve NP bileşeni sırasıyla Numerik Değerlendirme Skalası (NRS) ve Douleur Neuropathique 4 (DN4) anketleri kullanılarak değerlendirildi.

**Bulgular:** Torakotomi sonrası şiddetli PTAS sıklığı ise %19,1 olarak bulundu. Numerik Değerlendirme Skalası 3-10 arasında olan hastaların ise %53'ünde NP vardı. Ağrı şiddeti arttıkça NP sıklığı ve analjezik ilaç tüketimi artmıştır ($p<0,05$). Risk faktörleri olarak araştırılan; cinsiyet, yaş, operasyon süresi ve epidural analjezi uygulanmış olmasının PTAS ve NP sıklığı ve şiddeti üzerinde anlamlı bir etkisi bulunmadı. Hastalarda operasyon sonrası geçen süre arttıkça, PTAS sıklığı, nöropatik ağrı sıklığı ve ağrı şiddetinde azalma gözlendi ($p<0,05$).

**Sonuç:** Torakotomi ile cerrahi geçiren hastaların yaklaşık beşte birinde uzun dönemde şiddetli kronik ağrı tespit edilmiştir. Ağrının nöropatik bileşeni ağrı şiddeti arttıkça artmakta, ameliyattan sonra geçen zaman uzadıkça azalmaktadır. Etkin bir analjezi sağlanarak PTAS ve NP gelişimi azaltılmalıdır.

**Anahtar sözcükler:** Torakotomi, kronik ağrı, post-torakotomi ağrı sendromu, nöropatik ağrı

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## INTRODUCTION

Thoracotomy describes an incision made in the chest wall to access the contents of the thoracic cavity. Chronic post-thoracotomy pain was first defined as "persistent intercostal pain" in soldiers during World War II (1). In 1986, the International Association for the Study of Pain (IASP) defined "chronic post-thoracotomy pain syndrome (PTPS)" as "pain that persists or recurs through the surgical incision at least two months after the thoracotomy" (2). Chronic pain that occurs as a result of nerve damage or dysfunction is called "neuropathic pain" (NP). Neuropathic Pain is pain that arises as a direct consequence of a lesion or disease effecting the somatosensory system. The incidence of PTPS (NP and no-NP) is 4.8-74.6% and 6-55% of these patients have neuropathic components (3). Although the mechanism of pain after thoracotomy is yet fully unknown, surgical trauma, intercostal nerve damage, inflammation, and hypersensitivity may be components of PTPS (4-8).

The PTPS can be somatic, neuropathic, or mixed pain which is usually described as aching and burning at the surgical site. The neuropathic component of pain begins with intercostal nerve damage and an inflammatory response at the surgical incision site. Neuropathic PTPS patients describe pruritus, tingling, hypoesthesia, and sensory loss in the surgical site detectable by NP questionnaires (6-9). Hyperalgesia in the first postoperative 48 hours reflects central sensitization which is a sign of chronic NP (8,10).

This study aimed to determine the incidence of PTPS, the neuropathic component of pain, and risk factors in patients who underwent thoracotomy.

## MATERIAL and METHODS

This prospective cohort study was performed after Clinical Research Ethics Committee approval (08.05.2013 B.10.4.İSM.4.06.68.49) at the Anesthesiology and Reanimation Department of Gazi University Faculty of Medicine Hospital. Hospital thoracic surgery and anesthesia records were scanned. Patients who underwent thoracic surgery via thoracotomy between January 2010 and May 2013 were included in the analysis. Patients with death records, those under 18 years of age, and patients with incomplete data were excluded from the study.

To standardize the tissue damage caused by the operation, patients who did not require thoracotomy such as those undergoing bronchoscopy, mediastinoscopy, and video-assisted thoracoscopic surgery, were omitted.

The flow chart showing the method of screening patients for the study is summarized in Figure 1. Patients who had undergone thoracotomy at least three months ago were contacted by phone to evaluate PTPS. The patients were informed about the study and informed consent was obtained. During the phone conversation, the patients were questioned whether they had pain in the thoracotomy area. Patients were investigated for pain incidence, pain severity, NP and analgesic consumption. Pain incidence and severity were evaluated by the Numerical Rating Scale (NRS 0-10: 0; no pain, 10 worst pain imaginable, NRS=0: No pain, NRS=1-2: Mild pain, NRS≥3: Severe pain) (11). Mild PTPS was considered NRS=1-2 and severe PTPS was considered NRS=3-10. The Douleur Neuropathique 4 (DN4) neuropathic pain questionnaire whose Turkish validity and reliability have been tested, was used to determine NP (12-15). According to DN4, one point was given for each of the following questions: burning, painful cold sensation, electric shock, tingling, pricking, numbness, itching, touch hypoesthesia, needle hypoesthesia, and brush allodynia in the area where neuropathic pain is defined. 4 points and above were accepted as NP (14,15). Patients were also investigated regarding analgesic consumption and the effect of pain on his quality of life were recorded.

### Statistical Analysis

Data was analyzed with Statistical Package for the Social Sciences (SPSS) 15.0 software. Variables were expressed with appropriate descriptive statistics (mean ± standard deviation, median, interquartile range, percentage, etc.). We assessed the normality of the distribution using Kolmogorov-Smirnov test. In statistical comparison, the chi-square test was used

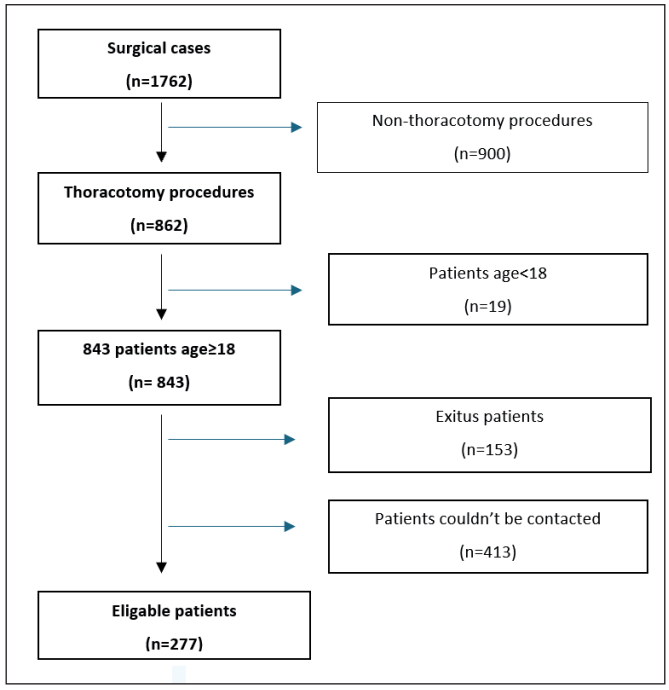


**Figure 1.** CONSORT diagram for patient selection.

for qualitative variables, t-test, Mann-Whitney U test and Kruskal-Wallis were used according to the suitability of quantitative variables. T test was used for continuous data with normal distribution and Mann-Whitney U test was used for data without normal distribution. Correlation and regression analysis were performed by bivariate correlation and Spearman test. Logistic regression and linear regression tests were applied depending on the data condition. In the study, $p<0.05$ was considered statistically significant.

## RESULTS

Demographic data, operation duration, presence of epidural analgesia, and analgesic consumption were presented in Table I. The mean operation time of the patients was 152.3 ± 71.6 minutes. Only 9.7% of patients with pain were using analgesics (Table I).

In 175 patients (63%) had no pain (NRS: 0), 49 patients (18%) had mild pain (NRS:1-2) and 53 patients (19%) had severe pain (NRS≥3). There was no correlation between pain severity and age. During the early postoperative period pain severity was higher (p=0.001, Table II). Sixty two percent of patients with severe pain (NRS 3-10) were on analgesics. Pain severity was strongly correlated with consumption of analgesic drugs (OR=2.9 p=0.0001 and OR=5.1 p=0.0001). No significant correlation was found between operation duration and pain severity (Table II).

Neuropathic pain assessed by DN4 was higher when NRS increased (p=0.0001) (Table II and III, Figure 2), logistic regression revealed 1.3 times increase (OR=1.3, CI:1.94-1.97). Pain severity was found to be 2.4 times higher for NP with logistic regression (OR=2.4, p=0.02) and was significantly positive correlated with DN4 score (OR=4.8, p=0.0001) (Table II). When evaluated according to pain severity, the neuropathic component occurred in 28 (53%) NRS≥3 patients and 6 (12%) NRS 1-2 patients. Patients with NP had significantly higher NRS scores (p=0.001) (Table III, Figure 2).

**Table I.** Demographic Data, Operation Time, and Analgesia Data

| | |
|---|---|
| Patients | |
| Male, n (%) | 212 (76.5) |
| Female, n (%) | 65 (23.5) |
| Age, mean ± SD | 57.8 ± 13.4 |
| Operation time (min), mean ± SD | 152.3 ± 71.6 |
| Epidural analgesia, n (%) | 64 (23) |
| Analgesic consumption, n (%) | 27 (9.7) |

**Table II.** Evaluation of Chronic Pain Severity and Related Factors

| | Pain severity | | | |
|---|---|---|---|---|
| | NRS 0 | NRS 1-2 | NRS 3-10 | p |
| Male/Female, n | 140/35 | 36/13 | 36/17 | 0.05 |
| Age (year)<br>Median (IQR) | 60 (15) | 57 (20.5) | 58 (14) | 0.332 |
| Evaluation time (month)<br>Median (IQR) | 42 (18) | 28 (10.5) | 35 (19.5)* | 0.001* |
| DN4 score<br>Median (IQR) | 0 (0) | 2 (2) | 5 (4.5)* | 0.001* |
| Analgesic consumption, n<br>Present/None | 1/171 | 1/47 | 20/32* | 0.001* |
| Epidural analgesia, n<br>Present/None | 43/129 | 6/42 | 15/40 | 0,455 |
| Operation time (min)<br>Median (IQR) | 145 (60) | 150 (60) | 120 (86.5) | 0.469 |

**NP:** Neuropathic pain, **NRS:** Numeric Rating Scale, **DN4:** Douleur Neuropathique 4, **min:** minutes, **IQR:** Interquartile range,
*: p<0.05, NRS 3-10 patients compared with NRS 0 and NRS 1-2 patients.

**Table III.** Evaluation of Pain Severity and Douleur Neuropathique 4 Scores

| Pain severity | NRS 0 | | NRS 1-2 | | NRS≥3 | |
|---|---|---|---|---|---|---|
| | DN4<4 | DN4≥4 | DN4<4 | DN4≥4 | DN4<4 | DN4≥4 |
| Patients, n (%) | 170 (98.3) | 3 (1.7) | 45 (88) | 6 (12) | 25 (47) | 28 (53) |

**NRS:** Numeric Rating Scale, **DN4:** Douleur Neuropathique 4.

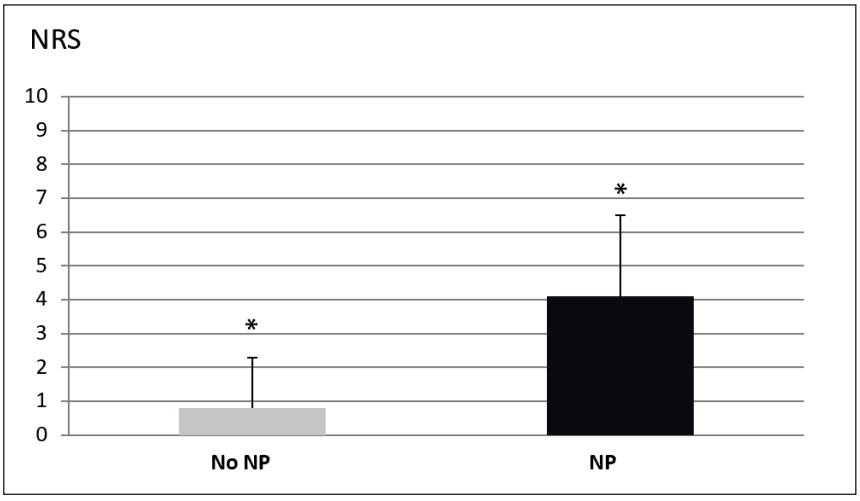


**Figure 2.** Evaluation of neuropathic pain according to pain severity.

**NP:** Neuropathic pain, **NRS:** Numeric Rating Scale, ***:** p<0.05: Between NP and no NP groups.

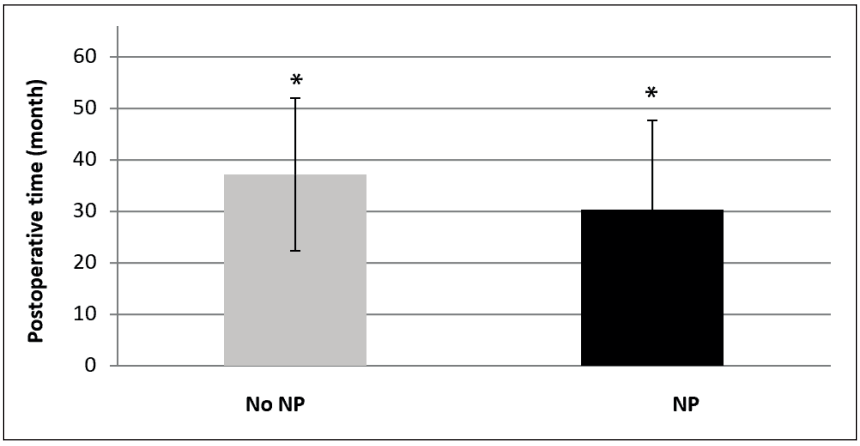


**Figure 3.** Evaluation of neuropathic pain due to postoperative time.

**NP:** Neuropathic pain, ***:** p< 0.05 Between NP and No NP groups.

Neuropathic pain-related factors were summarized in Table IV. It was observed that the incidence of NP varied depending on the postoperative evaluation time. The longer the postoperative evaluation period, the lower the incidence of NP was found (p=0.012). Neuropathic pain was more frequent when the NRS was higher and drug consumption was higher (Table IV, Figures 2 and 3). There was no relationship between NP and age or gender. No medication was used by 62% of patients with NP (Table IV). Ten patients (27%) expressed that NP altered their quality of life.

## DISCUSSION

In the present study severe PTPS frequency after thoracotomy operations was found to be 19.1 %, and 53% of these patients have NP. The incidence of PTPS varied between 4.8-74.6% in the literature and 6-55% of these patients have neuropathic components (3). This inconsistency among the results in the studies may be attributed to the design of studies, the homogeneity of the patients, anesthesia and analgesia protocols, pain assessment scales, and postoperative evaluation times (6,16).

The pain severity increased with the incidence of NP and was also correlated with the DN4 score. The early postoperative period was the most susceptible time for NP, on the contrary, the severity of pain and NP decreased after postoperative 36 months.

There are many questionnaires to detect NP by history and physical examination such as ID pain questionnaire, Neuropathic Pain Scale, Leeds Assessment of Neuropathic Symptoms and Signs, Neuropathic Pain Questionnaire (NPQ), and pain DETECT (17). To determine NP in our study, we preferred the Neuropathic Diagnostic Pain Questionnaire 4 (DN4) which is short and easy to apply, and whose Turkish validity and reliability have been investigated (15). Additionally, this method may be useful for self-assessment via phone interviews (14,17). When the cut-off score is 4, DN4 has the highest sensitivity and specificity and was found highly diagnostic in NP (12-15).

Neuropathic components have been shown in 5.9-55% of patients in post-thoracotomy pain studies (3). In our study, 53% of patients with severe chronic pain had a neuropathic

**Table IV.** Documentation of Neuropathic Pain Related Factors

| | No NP | NP | p |
|---|---|---|---|
| Male/Female, n | 183/57 | 28/9 | 0.9 |
| Age (year)<br>Median (IQR) | 60 (15) | 55 (14.5) | 0.2 |
| Evaluation time (month)<br>Median (IQR) | 37 (20) | 28 (32)* | 0.01* |
| NRS<br>Median (IQR) | 0 (1)* | 4 (3.5)* | 0.001* |
| Analgesic consumption, n<br>Present/none | 14/226 | 13/24* | 0.001* |
| Epidural analgesia, n<br>Present/none | 56/185 | 8/28 | 0.98 |
| Operation time (min)<br>Median (IQR) | 142.5 (60) | 135 (105) | 0.9 |

**NRS:** Numeric Rating Scale, **min:** minutes, **IQR:** Interquartile range, **NP:** Neuropathic pain. ***:** p<0.05: Between NP and no NP groups.

component, similar to Steegers et al (18). In addition, some studies confirm neuropathic PTPS patients have severe pain, hypoesthesia, and electrical shock while non-neuropathic PTPS patients have milder pain and hypoesthesia (5,19). Similarly, in our study, it has been shown that patients with severe pain had more NP.

There are some studies that the incidence of pain is higher in females and younger patients (18-21). However, there was no relation between pain severity and age or gender of patients, in our study. This might be due to a lower number of females in our study.

There was a correlation between postoperative evaluation time and pain intensity or NP. The severity of pain was found to be higher in patients in the early period after the operation. Also, the incidence of NP was found to be higher in patients who were questioned for pain in the early period, which is similar to other studies (16,22).

Muscle damage, nerve damage, rib fracture, chest tube insertion, and damage of costovertebral joints in thoracotomy operations are causes of PTPS. Nerve damage is a key risk factor in PTPS and other persistent postoperative pain syndromes (23). In thoracotomy operations, it is thought that long-term compression or interruption of the intercostal nerve with the retractor may be the cause of NP (24,25). Our records did not include detailed information about nerve dissection or rib retractor time. However, according to our findings, no correlation was found with the duration of surgery. So, in our study, similar to the literature, the duration of the operation was not a significant risk factor in NP (25).

In the early postoperative period, to prevent acute pain, regional analgesia (thoracic epidural, intercostal nerve block, intrapleural analgesia, wound infiltration, paravertebral block, erector spine plane block, serratus anterior plane block) and systemic analgesia (opioids, NSAIDs, acetaminophen) are used (26,27). Pain can be controlled with epidural local anesthetic drugs via thoracic epidural analgesia. However, there was no relationship between PTPS and thoracic epidural analgesia in our findings, similar to the literature. Also, the number of patients with epidural catheters and NP were not related (28). In our clinic, the routine protocol in thoracic surgery during that period was propofol and remifentanil infusion. Song et al. found the combination of propofol and remifentanil to be advantageous to chronic PTPS (29). However, we did not investigate the effect of anesthetic agents in this study.

There are some limitations of this study: Although the number of patients was initially high, the inability to reach all the patients may have affected the outcome of our study. Especially cancer patients with a shorter survival they may have not been contacted. Also, the effects of treatments such as chemotherapy and radiotherapy may have affected pain assessment. Patients were called only once at different times postoperatively. However, if it were possible to evaluate the same patient repeatedly, our results might have been more reliable.

Recent analgesia methods fascia plane blocks such as erector spina plane block and serratus anterior plane block were not used in this study. Investigation of the effect of these blocks is also needed for PTPS.

## CONCLUSION

This study showed that PTPS is a serious complication that occurs in approximately one in five patients who have undergone thoracotomy and half of them have NP. The neuropathic component of pain increases as pain intensity increases and decreases as time passes after surgery. The development of PTPS and NP should be reduced by providing effective analgesia. New strategies are needed to further decrease PTPS.

## AUTHOR CONTRIBUTIONS

**Conception or design of the work:** OE, LK, IT, DA
**Data collection:** OE, LK, IT, DA
**Data analysis and interpretation:** OE, LK, IT, DA
**Drafting the article:** OE, LK, IT, DA
**Critical revision of the article:** OE, LK, IT, DA
The author (OE, LK, IT, DA) reviewed the results and approved the final version of the manuscript.

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