Prevalence, Characteristics and Impact of the Post-Thoracotomy Pain Syndrome on Quality of Life: A Cross-Sectional Study

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Abstract

Background: Post-thoracotomy pain syndrome (PTPS) is relatively common with a varying prevalence of up to 80%. The objective of this study was to describe the prevalence, characteristics and impact of PTPS on quality of life among patients who underwent surgery either by open thoracotomy or video-assisted thoracoscopic surgery (VATS) due to lung cancer.

Methods: A questionnaire designed for the purpose of this study was sent to 200 consecutive patients who underwent surgery for lung cancer at Aalborg University Hospital between December 2008 and April 2012. Patients reporting pain were asked to fill out four validated questionnaires; short-form McGill Pain Questionnaire, Neuropathic Pain Symptom Inventory, Short Form 36-Item Health Survey, and the PainDETECT questionnaire.

Results: Data were ultimately analysed from 133 patients. The overall prevalence of PTPS was 29% and there was no significant difference in prevalence following thoracotomy and VATS (30% vs. 24% respectively; p=0.65). Neuropathic pain symptoms were found in 95% of PTPS patients. Acute post-operative pain (p< 0.01) and duration of hospital stay (p<0.05) were most often seen in patients who developed PTPS. Patients with PTPS had significantly lower quality of life than patients without PTPS (p<0.01).

Conclusion: The prevalence of PTPS is relatively following thoracic surgery due to lung cancer without any difference between open surgery and VATS. Furthermore, PTPS has a great impact on daily living, and patients with PTPS have a significantly lower quality of life compared with patients without PTPS. Neuropathic pain symptoms were reported in nearly all of the PTPS patients. There is a need for large randomized studies to provide a better insight into development of PTPS in open thoracotomy vs. VATS.

Keywords: Thoracotomy; Thoracoscopic surgery; Post-thoracotomy pain; Quality of life

Introduction

Chronic pain can emerge after surgery and is known as persistent post-surgical pain. Post-thoracotomy pain syndrome (PTPS) is defined as pain that recurs or persists along a thoracotomy scar at least two months after the surgical procedure [1]. This condition is relatively common and the prevalence of PTPS has been reported to be up to 80% [2]. In the majority of patients, pain is often mild and might only slightly interfere with normal daily activities. However, in some patients, pain can be severe and has a disabling impact on the quality of the patients' lives [2,3]. Furthermore, neuropathic pain characteristics are experienced by some patients following PTPS [4-6]. The pathogenesis of PTPS is still not clear and is most likely multifactorial. Trauma to intercostals nerve during thoracotomy has been suggested as a prerequisite for the development of PTPS [7,8]. Video-assisted thoracoscopic surgery (VATS) is a minimally invasive procedure and has been expected to reduce the prevalence of PTPS, but studies have shown conflicting results with regard to reducing the incidence of PTPS [3,4,9]. There is obviously still a lack of knowledge whether VATS confer less long-term postoperative pain than conventional open surgery for lung cancer and to what degree PTPS impacts postoperative quality of life. Additionally more insight into the type of pain is needed. Hence, the main objectives of this study were to examine the prevalence of PTPS following antero- or posterolateral thoracotomy and VATS in a sample of lung cancer patients in the North Denmark Region and to assess PTPS characteristics, including neuropathic pain symptoms. Furthermore, we aimed to investigate whether and how PTPS affects quality of life.

Materials and Methods

Design and study population

This study was a cross-sectional study that included a self-administrated questionnaire and collected information from available medical records.

Between December 1, 2008 and April 30, 2012 a total of 348 patients underwent thoracotomy or VATS for lung cancer at Aalborg University Hospital, Denmark which is a university affiliated hospital serving the North Denmark Region with approximately 580,000 inhabitants. A questionnaire was designed by the primary author and sent by ordinary mail to 200 consecutive surviving patients who had undergone thoracotomy or VATS for lung cancer in our hospital during the study period. As we were not able to perform any specific power calculation based on previous results from studies using questionnaires as mentioned below we arbitrarily set out to study 200 patients who underwent surgery for lung cancer. Patients who underwent surgery from April and backwards in time were contacted until 200 patients were included according to the in- and exclusion criteria mentioned.

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below patients were included in the study according to the following criteria: >18 years old, history of at least six months post-thoracotomy, and radically operated lung cancer. The six months was chosen in order to ensure the development of chronic pain. Patients with TNM stage of >N1 and/or >M0 after surgery and patients with any concomitant disease that could give rise to pain in the thoracic area were excluded from the study. The TNM Classification of Malignant Tumors is a cancer staging system that describes the extent or severity of a person's cancer. It is based on the size of the primary tumor (T), the amount of spread to lymph nodes (N), and the presence of metastasis (M). Based on the International Association for the Study of Pain [1], the current study defined PTPS as pain persisting either continuously or intermittently for six months or more after surgery and different from the preoperative pain. The study was approved by the Danish Data Protection Agency (2008-58-0028). Since this study was a non-interventional study, it did not require approval from local ethics committee.

**Questionnaires**

Enclosed with the questionnaire was a cover letter explaining the purpose and the methods of the study and requesting participation. The questionnaire included questions investigating current pain related to their surgery and whether they had pain before surgery and if so, if their current pain status differed from previous pain states. They were also asked if they had received radio- or chemotherapy before and/or after surgery. Patients with chronic pain were asked about use of analgesics, and their current pain intensity was assessed using a numeric rating scale (NRS) 0–10. Patients reporting chronic pain were also asked to fill out the short-form McGill Pain Questionnaire [10], Neuropathic Pain Symptom Inventory (NPSI) [11], and Short Form 36-Item Health Survey (SF-36) [12]. Furthermore, the PainDETECT questionnaire [13] was used to characterize pain course and intensity.

A telephone call was made to non-responders and to participants returning incomplete questionnaires. Contact by telephone was attempted up to three times if patients did not answer or returned an incomplete questionnaire within 1 month by ordinary mail.

**McGill pain questionnaire**

The short form McGill Pain Questionnaire includes a list of words, which patients can use to describe their subjective pain experience [10]. The words are arranged into 20 categories that can be divided into four major classes; sensory, affective, evaluative, and miscellaneous. The sensory category includes words that describe the sensory qualities of pain, e.g. stabbing, itching, and burning. The affective category included words such as sickening, frightful, and cruel. The evaluative category includes words that describe the overall intensity of their total pain experience, e.g. annoying and troublesome. The miscellaneous includes sensory, affective, and evaluative words.

**Neuropathic pain symptom inventory**

This questionnaire includes 12 items; 10 symptoms most commonly described by neuropathic patients (burning, pressure, squeezing, electric shocks, stabbing; pain evoked by brushing, pressure, or cold; tingling, pins and needles) and two items assessing the duration of spontaneous and paroxysmal pain [11]. The 10 symptoms can be divided into five dimensions: burning (superficial) pain, pressing (deep) pain, paroxysmal pain, evoked pain, and paraesthesia/dysaesthesia. Intensity of each symptom is rated on a numerical scale 0-10.

**Short form 36-item health survey**

This survey consists of 36 items that address health related quality of life [12]. This questionnaire measures eight dimensions of health status; Physical Functioning, Role Limitations - physical problems, Bodily Pain, General Health, Vitality, Social Functioning, Role Limitations - emotional problems, and Mental Health. For each dimension, a score is calculated with a possible total of 100. A total score is calculated as a mean of the eight dimensions with higher scores indicating better functioning.

**PainDETECT**

PainDETECT was developed firstly as a screening tool for neuropathic pain in musculoskeletal pain conditions [13]. However, the questionnaire has only been validated in patients with muscular-skeletal disorders, and was, therefore, not used as a screening tool in this study. Thus, no score was calculated based on this questionnaire, but data regarding pain course, radiating pain, and pain intensity are presented.

**Patient characteristics**

Following data were extracted from the patients' electronic medical records: age, gender, date of surgery, duration of hospital stay, side of surgery, TNM classification, operative procedure (thoracotomy or VATS), extent of surgery (wedge resection, lobectomy, bi-lobectomy, or pneumonectomy, decortications, and thoracic wall resection).

**Statistical analysis**

Continuous normally distributed data are presented with mean and standard deviation (SD) and continuous non-normally distributed data are presented with the median and interquartile range (IQR). Numerical data were analysed using unpaired t-test (normal distribution) or Mann–Whitney’s U test (non-normal distribution). Categorical data were analysed using Pearson's Chi-squared test. All statistical analyses were performed in R (R Foundation for Statistical Computing, Vienna, Austria) version 2.15.3. P-values ≤0.05 were considered statistically significant.

**Results**

**Patients**

During the study period 348 patients underwent surgery for lung cancer. Death (all causes) at study time left 268 patients for potential inclusion. Figure 1 illustrates the recruitment process of participating patients. A total of 52 among the included patients had undergone VATS and 148 patients had open surgery. Data were analysed from 133 patients (participation rate: 66.5%). There were no significant differences between participants and non-participants regarding gender, age, surgical approach, age, or time since surgery (data not presented). Concerning patients undergoing open surgeryotomy and VATS, the only significant difference was the length of hospital stay, where patients undergoing classic thoracotomy had a longer hospital stay (p<0.01). Patient characteristics are summarized in Table 1.

**Prevalence and characteristics of post-thoracotomy pain syndrome**

In total, thirty-eight patients (29%) reported having chronic pain related to their thoracic surgery and mean pain duration was 21.7 months. The prevalence of pain ranged from 44% at 6–12 months to 16% at 42–48 months after the surgery.

The most common pain course was "persistent pain with slight fluctuations" (42%) and "pain attacks without pain between them" (39%) (Table 2). Fourteen patients (37%) had radiating pain.
Median pain intensity of acute pain was 5 (IQR: 4.75) and mean current pain was 2.8 (SD: 2.4) on the NRS.

Twenty-one patients (55%) took medication for chronic pain including paracetamol (n=20), opioids (n=17), NSAIDs (n=4), gabapentin (n=1), and pregabalin (n=1). One patient reported using physiotherapy in addition to pain killers for pain management.

The McGill Pain Questionnaire was used to explore the patients’ subjective experience of their pain. All PTPS patients completed the questionnaire. The mean number of descriptive words chosen was 6.9 (SD: 5.2). The most common terms selected to describe the pain were sensory words, e.g. shooting, crushing, and aching. The three most frequently descriptors used were “annoying” (18/37), “shooting” (14/37), and “stabbing” (14/37).

Neuropathic pain symptoms

All PTPS patients completed the questionnaire. Of the 38 patients with PTPS, 36 (95%) experienced neuropathic pain characteristics (NPSI score>0) [11]. The intensity and proportion of patients reporting each neuropathic pain symptom are shown in Table 3. Pressing (deep) pain (symptoms of squeezing and pressing) was the most common reported term (69%), followed by evoked pain (pain evoked by pressure, brush or cold) (61%). Paresthesia/dysesthesia (tingling and pins and needles) was seen in 56% of patients, and paroxysmal pain (symptoms of stabbing and electric shocks) in 53%. Burning (superficial) pain was seen in 22% of the patients with PTPS.

Predictors of post-thoracotomy pain syndrome

Acute post-operative pain measured by VAS was significantly higher in patients with PTPS than those without chronic pain (p<0.01). Furthermore, patients with PTPS had a longer hospital stay than patients with no chronic pain (p=0.05).

There were no significant differences between patients with and without PTPS concerning gender or age at the study, age at the surgery, time since the surgery, operation side, operational procedure, extent of surgery, postoperative outcome, pre- or postoperative radiotherapy/chemotherapy, TNM stage, or preoperative pain (Table 4).

Quality of life

Quality of life was measured using the SF-36 questionnaire. The questionnaire was completed by 131 patients (98.5%). The mean total score was 47 (SD: 21) for patients with PTPS and 69 (SD: 21.5) for patients without PTPS (p<0.01). Table 5 shows dimension scores and total scores for patients with and without PTPS. The postoperative SF-36 score for each dimension of patients with PTPS was significantly lower than for patients without pain. There were no significant differences in total scores or in the eight dimension scores for patients undergone VATS and thoracotomy.

Discussion

The primary findings of the present study was identification of a prevalence of PTPS at 29% within the study population, without significant difference according to surgical procedure (thoracotomy and VATS).
The prevalence of post-thoracotomy pain syndrome (PTPS) identified in the present study is among the lowest compared with findings of other studies where prevalence has been reported up to 80% [14]. However, differences between definitions of PTPS [14] make comparisons of studies difficult. In addition, mean time since surgery also differs between studies and has an important influence on the prevalence of chronic pain. Although time since surgery was not a significant contributor to PTPS in this study, the prevalence of PTPS in the first year after surgery was approximately twice as high as the prevalence of PTPS after 42-48 months (although the difference is not significant; p=0.1), thus suggesting that the prevalence is descending over time.

When comparing VATS and thoracotomy there was no significant difference in the prevalence of PTPS (30% vs. 24%; p=0.65). However, hospital stay was shorter for patients who had VATS, suggesting that this procedure might cause fewer complications postoperatively. This is supported by the results of this study where 28% of patients with PTPS had post-surgical complications compared to 14% of patients without PTPS, although the difference is not significant. Previous studies investigating the advantages of VATS in regard to PTPS have shown conflicting results [3-5,15-17]. A prevalence of 40% for patients undergoing thoracotomy and 47% for patients undergoing VATS has been found, but the difference was not significant [4]. Furthermore, another previous study found no significant difference in PTPS prevalence, distribution of pain, sensory changes, or effect of pain on daily activities between classic thoracotomy and VATS. However, a lower prevalence of PTPS in patients undergoing VATS compared with those having classic thoracotomy (30% vs. 44%) has also been reported [9]. In this case, the difference in PTPS prevalence was only significant within the first year after surgery. These results suggest that PTPS is a consequence of not only intraoperative factors in the long term.

### Neuropathic pain symptoms

Out of the 29% of patients with PTPS, 95% had neuropathic pain symptoms in the area of surgery, although the intensities measured on the NRS were quite low. The most frequently experienced symptoms were spontaneous feeling of pressure (58%), pressure-evoked pain (56%), and abnormal sensation of pins and needles (53%). Even though the intensity of neuropathic pain symptoms and of the general pain was relatively low (<2.7 and 3.7 on NRS), more than half of PTPS patients took medication for their pain.

The occurrence of neuropathic pain symptoms in the current study is the highest reported in the literature but it should be noted that some of these patients might have only experienced a single neuropathic pain symptom. The prevalence of each neuropathic symptom obtained from Leeds Assessment of Neuropathic Symptoms and Signs Pain Scale has been found to be between 35.2 and 82.8% [15], and another study found a neuropathic pain component in 35.7% of chronic pain patients [18]. Neuropathic pain has also been reported to be present in 23% of the patients with chronic pain following thoracic surgery [4].

The high frequency of neuropathic pain symptoms in this study does not provide direct information regarding prevalence of neuropathic pain, since such a diagnosis should be made based on a combination of neuropathic pain questionnaires and clinical assessments of nerve function. Therefore, it cannot be concluded that PTPS is a result of nerve damage based on the present results. In addition, pain-free patients may also experience neuropathy, which does not necessarily have to be painful. A previous study found that 25% of pain-free patients had sensory changes (defined as “any altered or uncomfortable mechanical skin sensations relating to thoracic surgery”) in the thoracic area [3]. Current screening-tools only allow patients to report neuropathies associated with pain, and the incidence of nerve damage may, therefore, be underestimated. This aspect should be considered in future studies.

### Quality of life

This study is one of a very few looking at both mental and physical quality of life after thoracic surgery. For this purpose, a validated Danish translation of SF-36 was applied in both PTPS patients and non-PTPS patients. The total scores for patients with PTPS were significantly lower than scores for patients without PTPS. In addition, patients without PTPS had significantly higher scores in all eight health dimensions. To our knowledge, this is the first study to report differences in mental health, vitality, and social functioning in patients with and without pain following thoracic surgery.

Previous studies have investigated the consequences of PTPS on activities of daily living [2,3,15,18]. SF-36 has previously been used to evaluate health related quality of life [6]. In contrast to the results of the present study, they only found significant difference between patients with and without pain in regard to physical functioning and body pain [6]. It has been shown that chronic pain following thoracotomy interfere with daily life in more than 50% of patients [2] and daily activities is impaired by pain in more than 60% of PTPS patients [3]. The findings of the present and previous studies support the fact that even though the PTPS patients experience mild pain, the pain is nonetheless affecting quality of life and, thus, can result in socioeconomic consequences.

**Table 3: Proportion of post-thoracotomy pain syndrome patients reporting neuropathic pain symptoms (NPSI >0) and mean intensity of symptoms scored from 0 to 10 on a numerical scale.**

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>N (%)</th>
<th>Mean intensity (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Spontaneous pain</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burning</td>
<td>8 (22)</td>
<td>0.9 (2.2)</td>
</tr>
<tr>
<td>Squeezing</td>
<td>15 (42)</td>
<td>1.8 (2.7)</td>
</tr>
<tr>
<td>Pressure</td>
<td>21 (58)</td>
<td>2.3 (2.5)</td>
</tr>
<tr>
<td><strong>Pain attacks</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electric shocks</td>
<td>5 (14)</td>
<td>0.5 (1.5)</td>
</tr>
<tr>
<td>Stabbing</td>
<td>16 (44)</td>
<td>2.4 (3.0)</td>
</tr>
<tr>
<td><strong>Evoked pain</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brush-evoked pain</td>
<td>11 (31)</td>
<td>1.4 (2.4)</td>
</tr>
<tr>
<td>Pressure-evoked pain</td>
<td>20 (56)</td>
<td>2.6 (3.1)</td>
</tr>
<tr>
<td>Cold-evoked pain</td>
<td>9 (25)</td>
<td>0.9 (2.1)</td>
</tr>
<tr>
<td><strong>Abnormal sensations</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tingling</td>
<td>14 (39)</td>
<td>1.2 (1.9)</td>
</tr>
<tr>
<td>Pins and needles</td>
<td>19 (53)</td>
<td>2.0 (2.4)</td>
</tr>
</tbody>
</table>

Abbreviations: SD: Standard Deviation.
Predictive factors of post-thoracotomy pain syndrome

In the present study we did not try to identify predictive factors of PTPS due to the low number of participants. However, we noticed that the only two factors that were significantly different between PTPS patients and those without PTPS were acute post-operative pain and duration of hospital stay. The acute pain was measured by asking the patients to score the intensity of pain they felt the first days after the operation on a VAS scale. This parameter is, of course, confounded by a potential recall bias. In addition, the higher intensity of acute pain reported by patients with PTPS could be a result of psychological factors as well as their current pain status, rather than an actual relationship between acute pain and PTPS.

Previous studies have reported predictive factors including younger age, female gender, acute post-operative pain, extensive surgery, diabetes mellitus, duration of chest tube drainage, higher post-operative white blood cell count, and pre-existing hypertension [4,6,14].

Table 4: Predictive factors for the prevalence of post-thoracotomy pain syndrome.

<table>
<thead>
<tr>
<th>Predictive factors of post-thoracotomy pain syndrome</th>
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</table>
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Table 5: SF-36 Health Survey scores for patients with and without post-thoracotomy pain syndrome.

<table>
<thead>
<tr>
<th>SF-36 scales</th>
<th>PTPS (n=93)</th>
<th>No pain (n=38)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical functioning</td>
<td>47.4 (21.7)</td>
<td>69.2 (25.4)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Role limitations – physical problems</td>
<td>20.4 (32.3)</td>
<td>54.0 (41.9)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>52.0 (25.4)</td>
<td>81.0 (26.1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>General health perception</td>
<td>44.4 (21.0)</td>
<td>63.2 (21.8)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Vitality</td>
<td>40.5 (21.1)</td>
<td>58.2 (24.9)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Social functioning</td>
<td>64.6 (31.4)</td>
<td>83.0 (24.7)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Role limitations – emotional problems</td>
<td>42.1 (42.2)</td>
<td>68.1 (40.8)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Mental health</td>
<td>66.4 (20.5)</td>
<td>76.0 (22.5)</td>
<td>0.02</td>
</tr>
<tr>
<td>Total score</td>
<td>47.2 (21.0)</td>
<td>69.1 (21.5)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Abbreviations: PTPS: Post-Thoracotomy Pain Syndrome; SF-36: Short Form 36. Data are presented with mean and standard deviation.
Preoperative pain has been shown to be a risk factor for persistent pain in several types of surgery [19-21], but only few studies on PTPS has assessed preoperative pain and these have shown conflicting results [14,22,23]. The role of preoperative pain in the development of chronic pain following thoracic surgery should be considered in future studies.

Post-operative use of analgesics

Half of the patients with PTPS used analgesics for their pain following surgery. Surprisingly, 81% of the patients using analgesics took opioids (17/21), which are normally used for moderate to severe pain. This could indicate that the pain is disabling although reported as mild. Only 9.5% (2/21) used antineuropathic medication (gabapentin and pregabalin) in contrast to 95% with a neuropathic component according to NPSI. This is in accordance with a previous study which found that only 2% used antineuropathic medication in contrast to 23% with a neuropathic component according to the PainDETECT Questionnaire [4].

Study limitations

The design of the current study holds limitations that should be kept in mind. The current study estimated the prevalence of pain based on a self-reported pain by patients, which can be a potential bias to the results due to recall bias. Furthermore, the questionnaire constructed by the first author has never been validated on its own. However, questions asked were simple and we have no reason to believe that answers differ between surgical groups. Objective assessment of pain could support the self-reported data. The cross-sectional design of this study provides a point prevalence of PTPS estimated within a specific time point, and, therefore, some patients might not have developed pain yet, and some patients could have had chronic pain after surgery that have disappeared at the time of the study. In addition, the population of the study may not have been enough large to proof statistical significance.

Non-responders are another source of bias. If the prevalence of PTPS among the non-responders was high, this study might have underestimated the prevalence of PTPS and vice versa. The non-responders could also have different characteristics of pain than the participants in this study. In addition, patients with pain might be more willing to participate in such studies more often than patients without pain, in which case, the prevalence of PTPS is overestimated. However, the response rate in this study was 67%, which is above the mean response rate (60%) among mail surveys published in medical journals [24].

Future directions

A well designed and sufficiently powered randomized study with follow-up over a longer time period is necessary in order to obtain more valid estimates regarding development of PTPS comparing open thoracotomy with VATS in thoracic surgery.

Quantitative sensory testing should be performed in order to profile and characterise the sensory abnormalities in PTPS.

PTPS is a well-recognized clinical problem; however, the results of this study suggest that it also can have serious socio-economic consequences. Such should be investigated in future studies in order to avoid burden to patients and society.

Conclusion

The prevalence of PTPS is relatively frequent following thoracic surgery due to lung cancer, without any difference between open surgery and VATS. Furthermore, PTPS has a great impact on daily living, and patients with PTPS have a significantly lower quality of life compared with patients without PTPS.

PTPS occurred in 29% of patients, which confirms previous findings that PTPS is a relatively frequent complication following thoracic surgery. Furthermore, up to 95% of these patients had pain with neuropathic characteristics.

There is still a need for well powered randomized studies to compare development of PTPS following VATS and open thoracic surgery.

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