A retrospective study of open thoracotomies versus thoracoscopic surgeries for persistent postthoracotomy pain☆,☆☆

Harsha Shanthanna MDa,⁎, Dina Aboutouk MDa, Eugenia Poon MDa, Ji Cheng MScb, Christian Finley MDc, James Paul MDa, Lehana Thabane PhDa,b,d

aDepartment of Anesthesia, McMaster University & St. Joseph's Hospital, Hamilton, Ontario, Canada
bMcMaster University & The Research Institute, St Joseph's Hospital, Hamilton, Ontario, Canada
cDepartment of Surgery, McMaster University & Department of Thoracic Surgery, St Joseph's Hospital, Hamilton, Ontario, Canada
dDepartment of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada

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Abstract
Objective: Persistent thoracotomy pain syndrome (PTPS) is a recognized complication and is considered to be less after video-assisted thoracoscopic surgery (VATS) compared with open thoracic surgery (OTS). The primary objective was to compare the incidence of PTPS at 6 months. Secondary objectives were to compare the incidence of neuropathic pain between VATS and OTS and to report perioperative factors associated with the development of PTPS.

Methods: This historical cohort study involved patient contact by a questionnaire regarding the presence of PTPS and its type. Patient, surgical, and analgesia factors were collected from health records, acute pain, and thoracic surgery databases. The data were analyzed using a multivariable logistic regression analysis, with results reported as adjusted odds ratio (OR) (95% confidence interval; P value).

Results: Of 308 patients, 130 returned their questionnaire, and 106 responses were analyzed. The incidence of PTPS was 35% and 54% with VATS and OTS respectively, with an adjusted OR, 0.33 (0.13-0.86), P= .024. The percentage of neuropathic pain was 18% and 48%, with VATS and OTS respectively, with an adjusted OR, 0.18 (0.04-0.85), P= .031. The diagnosis of cancer and previous chronic pain history were observed to be significantly associated with PTPS.

Conclusions: Our study indicates that PTPS is significantly more common and has a higher chance of being neuropathic with OTS. Despite being relatively less traumatic, VATS still carries a significant potential for PTPS. A diagnosis of cancer and history of previous pain are highly predictive of its development.

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⁎ Corresponding author at: Department of Anesthesiology and Pain Medicine, St Joseph’s Hospital, McMaster University, 50 Charlton Avenue East, Hamilton, Ontario, Canada L8N 4A6. Tel.: +1 905 522 1155x33853; fax: +1 905 521 6019.
E-mail address: harshamd@gmail.com (H. Shanthanna).

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1. Introduction

Persistent thoracotomy pain syndrome (PTPS) is one of the most common complications after thoracic surgery [1]. Along with limb amputation, thoracotomies elicit the highest risk of severe chronic postoperative pain, defined by the International Association for the Study of Pain as pain that recurs or persists along a thoracotomy scar at least 2 months after the procedure [1,2]. It has been suggested that this definition is overly simplified, especially the consideration of 2 months, as most studies show a gradual decline in the incidence over time [3]. However, even when considered at 6 months after surgery, the incidence of PTPS has been shown to be close to 22% to 67% [4-6]. The factors contributing to this high incidence of PTPS are not entirely clear and are reasoned to include both surgical and nonsurgical factors. Surgical factors include kind of incision (muscle splitting vs muscle sparing), techniques of entering the pleural space, length of the surgery, and the use of intracostal vs paracostal sutures [7]. Suggested nonsurgical factors include age, genetic predisposition, psychosocial factors, diagnosis, and preexisting chronic pain (PCP) [7]. Video-assisted thoracic surgery (VATS) is a minimally invasive procedure. One of its advantages is the avoidance of muscle dissection and rib cutting, which could theoretically decrease the chances of PTPS. However, study reports in this area are conflicting. Some have shown a reduced incidence of PTPS with VATS [8], however, many others have shown similar incidences [9-11]. The underlying nature of PPTS is considered to be predominantly neuropathic, even if not entirely neuropathic. Maguire et al [10] elicited symptoms of neuropathic pain (NP) in 35% to 85% of patients with PTPS. Previous studies have used tools such as self-report version of the Leeds Assessment of Neuropathic Symptoms and Signs Pain Scale (S-LANSS) and PainDETECT to identify the presence of a neuropathic component in PTPS [10,12], and correlated it as the nature of PTPS. Although the use of thoracic epidural analgesia (TEA) in open thoracic surgery (OTS) has been observed to decrease the incidence of PTPS [13], the utility of TEA in VATS procedures is uncertain [14,15].

The primary objective of this study was to compare the incidence of PTPS between OTS and VATS. Secondary objectives were to assess the incidence of NP and compare between the 2 groups, and to determine for patient, surgical, and analgesia factors associated with the development of PTPS.

2. Materials and methods

Approval from McMaster Research Ethics Board was obtained to conduct a historical cohort study of lung surgery patients performed at St. Joseph’s Hospital, Hamilton. We included patients aged >18 years who had thoracic surgery (both elective and emergency) within the last 6 to 18 months, considered from a starting point of May 1, 2012. Patients were excluded if their preanesthetic consultation noted any psychiatric or cognitive dysfunction that would limit their participation; inability to communicate in English language; if they only had diagnostic procedures such as bronchoscopy, mediastinoscopy, or lung biopsy; or had both OTS and VATS procedures. All patients had multimodal analgesia consisting of either TEA or opioid-based patient-control analgesia, along with acetaminophen with anti-inflammatory medications. For patients of TEA, thoracic epidural catherization was performed in the preanesthetic block room, before the induction of general anesthesia. Based on our literature review, the baseline probability of PTPS in OTS and VATS was considered as 45% and 25%, respectively [4-6]. The power of the study (β) was set at 80%, with an acceptable α margin of .05. The calculations were done as a difference in proportions for an uncorrected χ² test using PS-Power and Sample Size Calculation Web application (version 3.0.43). For a 2-sided test, a sample size of 90 patients per group was estimated. Considering the challenges of a retrospective study and a possible lower rate of response, we estimated to include 125 patients per group in our initial contact. An analysis of previous 3 months revealed that we will be able to approach at least 15 patients/month (excluding nonlung and diagnostic procedures). Patients who had their surgery from May 2012 until October 2013 were included. Questionnaires were mailed out to patients, who had at least 6 months after their surgery from October 2013 until May 2014. List of patients was obtained from the thoracic surgery database. Initial contact was achieved by a mailed questionnaire. We inquired the presence or absence of pain related to surgical exposure, its intensity and type, and whether it necessitates analgesic medications. The intensity was recorded in a Visual Analogue Scale of 0 to 10 (0 = no pain; 10 = maximum pain), and type was assessed using S-LANSS questionnaire. A threshold of >3 in 0 to 10 Visual Analogue Scale was used to indicate the presence of PTPS. We also inquired about any preexisting pain in the same side of chest, or other parts of the body, its intensity, and preoperative exposure to regular opioid medications (defined as daily intake for at least 1 month before surgery). Nonresponders were contacted by a phone call 6 weeks after the questionnaire was mailed out. Demographical, surgical, and postoperative analgesia details were collected using health records, acute pain database, and the thoracic surgery databases. Primary outcome was considered as the incidence of PTPS (defined as pain at or around the incision area) lasting for at least 6 months postoperatively. The data were analyzed using a multivariable logistic regression analysis, with a generalized estimating equation model. The primary and secondary outcomes were expressed as adjusted odds ratio (OR) with 95% confidence intervals (CIs). The data were analyzed as adjusted OR as this was a nonrandomized study, and hence, there could be unequal distribution of known or unknown confounders. Covariables that were considered and adjusted within the analysis included age, gender, diagnosis (cancer/noncancer), history of PCP (either at the same site or elsewhere), history of preexisting opioid use, surgeon performing the surgery, type of surgery
(pneumonectomy, lobectomy, wedge resection), and the use of TEA for postoperative pain control.

3. Results

The patient flow diagram is shown in Figure. A total of 353 patients were initially approached; however, 11 patients were excluded because of selection criteria, and 34 patients were reported by the family as deceased. Of 308 valid patients, 130 patients returned their questionnaire (109 patients responded to our initial contact, and a further 21 patients responded after the reminder phone call) and 56 patients declined to participate citing various reasons. Our final response rate was 60%. Our final analysis included 106 patients, as 24 responses were incomplete and could not be analyzed for primary outcome. Demographical, medical, and surgical history were compared between the 2 groups using unpaired t test and are shown in Table 1. The VATS group had significantly more wedge resections, whereas a large proportion (92%) of OTS was for cancer surgeries compared with 74% in VATS. The use of TEA was found to be 82% in OTS compared with 44% in VATS. One of the 3 surgeons performed relatively larger number of OTS (as he mostly performed more extensive surgeries). Other patient characteristics were found to be similar between the 2 groups. Results are summarized in Table 2.

3.1. Incidence of PTPS

Of 106 patients, 22/60 (36.7%) had presence of PTPS after VATS at 6 months after surgery, compared with 25/46 (54.4%) after OTS. After adjusting for prespecified covariates and treating surgeons as a cluster, the OR with 95% CI was 0.35 (0.12-1.01), \( P = .052 \). When analyzed with a reduced model by only including covariates with a \( P \leq .2 \), the OR was observed to be 0.33 (0.13-0.86), \( P = .024 \).

![Study Flow Diagram](image)
3.2. Incidence of NP

Among patients with PTPS, 16 patients had NP (assessed as a score of ≥12 in S-LANSS). Four (18%) of those patients had VATS, and 12 (48%) had OTS. An adjusted logistic regression analysis showed an OR of 0.21 (0.04-1.19), \( P = .077 \). When covariates only with a \( P \leq .2 \) were included, OR was 0.18 (0.04-0.85), \( P = .031 \).

3.3. Factors associated with development of PTPS

Among patient and surgical factors, the diagnosis of cancer (OR = 0.17 [0.04-0.75]; \( P = .019 \)) and history of previous chronic pain (OR = 3.52 [0.996-14.01]; \( P = .051 \)) were observed to be significantly correlated with the development of PTPS. Use of epidural analgesia was not shown to be associated with PTPS (OR = 0.88 [0.31-2.55]; \( P = .338 \)).

4. Discussion

Our historical cohort study demonstrates that the odds of developing PTPS are 33% less with VATS compared with OTS. It also shows that the odds of PTPS being neuropathic in nature are more with OTS. Use of TEA was not shown to be associated with PTPS. However, patients with a diagnosis of cancer and history of PCP are more prone to develop PTPS.

A total of 130 questionnaires were sent back to us, and 56 patients declined the study. Our response rate of 60% could be considered relatively low compared with similar studies [10]. Other studies, which have specifically looked at response rate for postal surveys with a telephone follow-up, also observed a high rate of incomplete or partial responses[16]. Among the nonresponders, we observed many false contact addresses and phone numbers. Ours is a major tertiary care center, and many patients come from other surrounding areas with temporary arrangements for stay during the perioperative period. It is most likely that many patients did not get the questionnaire at all.

The average incidence of PTPS observed was 44.3% (47/106), which falls within the reported range. However, literature shows a wide variation in the reported incidences; 25% with Peng et al [17], 57% with Maguire et al [10], and 75% with Perttunen et al [6]. Considering the extent of injury involved with OTS compared with VATS, it is reasonable to assume that the chances of PTPS could be relatively higher[7] as observed in our study. Findings consistent with our observation have been previously reported by Landreneau et al [9] and Wildgaard et al [18]. However, a few other studies have reported similar incidence of PTPS between OTS and VATS [10,12]. Despite being minimally invasive, VATS can still involve intercostal nerve damage—due to trochar insertion and manipulation of scopes—which can crush the nerve against the rib and the possibility of a slightly longer surgical time [7]. However, the presence of intercostal nerve injury, suggested by qualitative sensory testing, failed to show any association with the presence of PTPS in another observational study [19]. Unfortunately, most existing randomized

### Table 1
Demographic, medical, and surgical variables compared between the 2 groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Open thoracic surgeries (n = 52)</th>
<th>Video-assisted thoracoscopic surgeries (n = 78)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Mean (SD) 67.3 (11.4)</td>
<td>66.0 (13.2)</td>
<td>.571</td>
</tr>
<tr>
<td>Gender: count (%)</td>
<td>Male 21 (40.4)</td>
<td>30 (38.5)</td>
<td>.826</td>
</tr>
<tr>
<td></td>
<td>Female 31 (59.6)</td>
<td>48 (61.5)</td>
<td></td>
</tr>
<tr>
<td>Surgical type</td>
<td>Wedge resection 6 (10.0)</td>
<td>23 (30)</td>
<td>.047</td>
</tr>
<tr>
<td></td>
<td>Lobectomy 34 (66.0)</td>
<td>40 (52.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Segmentectomy 6 (12.0)</td>
<td>10 (13.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Decortication 2 (4.0)</td>
<td>1 (1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Others 4 (8.0)</td>
<td>3 (4)</td>
<td></td>
</tr>
<tr>
<td>Diagnosis: count (%)</td>
<td>Cancer 48 (92.3)</td>
<td>58 (74.4)</td>
<td>0.010</td>
</tr>
<tr>
<td></td>
<td>Previous chronic pain count (%)</td>
<td>9 (18.0)</td>
<td>.596</td>
</tr>
<tr>
<td>Use of epidural analgesia count (%)</td>
<td>42 (82.4)</td>
<td>34 (44.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Surgeon performing: count (%)</td>
<td>Surgeon 1 16 (29.4)</td>
<td>33 (42.3)</td>
<td>.028</td>
</tr>
<tr>
<td></td>
<td>Surgeon 2 24 (47.1)</td>
<td>19 (24.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Surgeon 3 12 (23.5)</td>
<td>26 (33.3)</td>
<td></td>
</tr>
</tbody>
</table>

### Table 2
Summary of results

<table>
<thead>
<tr>
<th>Primary outcome</th>
<th>OTS incidence rate (%)</th>
<th>VATS incidence rate (%)</th>
<th>Adjusted OR with 95% CI</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent postthoracotomy pain syndrome</td>
<td>25/46 (54.4)</td>
<td>22/60 (36.7)</td>
<td>0.33 (0.13-0.86)</td>
<td>( P = .024 )</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NP</td>
<td>12/25 (48)</td>
<td>4/22 (18)</td>
<td>0.18 (0.04-0.85)</td>
<td>( P = .031 )</td>
</tr>
<tr>
<td>Diagnosis of lung cancer</td>
<td>42/46 (92)</td>
<td>44/60 (74)</td>
<td>0.17 (0.04-0.75)</td>
<td>( P = .019 )</td>
</tr>
<tr>
<td>History of preexisting pain</td>
<td>9/46 (19)</td>
<td>11/60 (18)</td>
<td>3.52 (0.996-14.01)</td>
<td>( P = .051 )</td>
</tr>
</tbody>
</table>

NOTE: Of 130 responses, 24 responses were incomplete and could not be analyzed for primary outcome.
controlled trials comparing VATS vs open surgery do not report on long-term pain outcomes [20].

Most studies in literature have observed a relatively higher incidence of NP compared with our study. This could have been the result of a smaller sample size. A systematic review looking at the NP component in persistent postsurgical pain observes that the prevalence of NP is highest with breast resection (67.7%) followed by thoracic surgeries (66%) [21]. However, there is again a wide variability in the reported figures. These variations could be due to the differences in scales (painDETECT, LANSS, etc) used to assess NP. Maguire et al [10] reported an incidence between 35% and 83%, whereas Steegers et al [12] reported the incidence of definite NP as 23%.

Although the use of postoperative TEA was significantly different between the 2 groups, it was not shown to be influencing the incidence of PTPS. A recent Cochrane review reported that TEA initiated preincision and continued postoperatively, decreased the chances of PTPS at 6 months [22]. However, a previous meta-analysis comparing preincision vs postsurgical TEA had demonstrated no protective benefit for the development of PTPS when initiated before incision [23]. However, all the involved studies in both reviews were done for open surgeries. The use of TEA with VATS is low, and there are no studies documenting the benefit that might be achieved with the use of TEA for PTPS in VATS.

Among other factors, history of PCP has been consistently linked with the development of persistent postsurgical pain. In the risk assessment score developed by Althaus et al [24], “preoperative pain in the operating field” and “other chronic preoperative pain” were identified as separate predictive factors among the 5 identified by multivariate logistic regression analysis. However, specific to PTPS, Wildgaard et al [7] note that the available information could be conflicting and limited because most studies have excluded such patients. But recent studies are in support of this finding [25]. Our finding of association of cancer diagnosis and persistent postsurgical pain has been observed by studies for both breast and lung cancer [26]. Cancer itself alters several local and humoral mediators, apart from other changes induced by chemo and radiotherapy treatments [27]. These changes make a patient more susceptible for PTPS.

Our study also had important limitations. Although we expected to achieve a sample size of 90 per group, we were unable to achieve it, which makes it prone for a biased result. Being retrospective, it was prone for recall bias. We compared the cohorts of VATS and OTS for PTPS without randomization. This possibly suffers from selection bias, as patients of OTS may have more advanced disease and other unidentified factors acting as confounders. We also did not include the duration of surgery and severity of acute postoperative pain, as previous studies have highlighted.

4.1. Future directions

Clearly, PTPS is a significant burden for patients of thoracic surgery. Although studies have identified some predisposing factors, we still do not understand the transition from acute pain to persistent pain. Future studies must aim to better study these factors. Future trials, apart from being prospective and controlled, must be of adequate size to allow for sufficient confidence in their results.

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References


