Original Article

Incidence of early persistent pain after video-assisted thoracoscopic surgery: a single-centre prospective cohort study

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Background: Despite the benefits of video-assisted thoracoscopic surgery (VATS), postoperative acute pain and nerve injury are still present and contribute to early persistent and chronic pain. The purpose of this study is to describe the incidence of early persistent pain (EPP) after VATS, which remains unexplored, to enhance patient care and promote awareness among clinicians regarding this clinical condition.

Methods: A single-center prospective cohort study that included consecutive patients undergoing VATS between January 2021 and March 2023. The primary outcome was the incidence of EPP, defined as pain experienced at 3 to 4 weeks follow-up. Secondary outcomes were risk factors associated with EPP, characteristics during physical examination, acute postoperative pain scores, the use of additional analgesia and complications between patients with and without EPP.

Results: Of 117 patients, 16.2% [95% confidence interval (CI): 9–23%] developed EPP. The presence of acute postoperative pain was the only risk factor for EPP. The pain was mostly localized at the utility and ventral incision. Hyperesthesia, hypoesthesia and a positive pinch test were the most common sensory disturbances. Patients with EPP showed significantly higher acute pain scores until postoperative day (POD) 4, more frequently used additional opioids until POD 2, and had comparable complications.

Conclusions: Early persistent postoperative pain is present in 16.2% of patients after VATS. Acute postoperative pain is the strongest risk factor for developing such persistent pain. This underlines that awareness of clinicians for strategies that optimize postoperative pain management is of utmost importance.

Keywords: Persistent postsurgical pain; video-assisted thoracoscopic surgery (VATS); acute postoperative pain; neuropathic pain

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Introduction

The introduction of video-assisted thoracoscopic surgery (VATS) has led to shorter hospitalization as well as decreased cardio-pulmonary complications (1). However, the association between VATS and immediate postoperative pain remains a subject of ongoing discussion and investigation, as surgical trauma and damage to the intercostal nerves remain (2). Optimal pain management in the acute phase after thoracic surgery is crucial as it significantly impacts patients' recovery and serves as an essential indicator for chronic pain (3). Chronic pain is defined as pain lasting for more than three to 6 months after surgery (4). Despite the benefits offered by VATS, a substantial proportion of patients continue to experience chronic pain, with a reported incidence of 11% 3 months after surgery, accompanied by pain-related functional impairment in approximately 30% (5). Notably, a study has demonstrated the association between acute and chronic pain in a multivariate model involving 490 patients who underwent thoracic surgery (thoracotomy and VATS combined), indicating that the severity of acute postoperative pain during the initial 3 days following surgery was the only factor associated with the presence of chronic pain at 6 months (2).

Various other features, such as ongoing inflammation, nerve damage and psychological factors, have been proposed as significant pathogenic factors contributing to chronic pain (4-6), demonstrating that patients with postoperative neuropathic pain experienced significantly more severe acute pain, necessitating additional analgesia and prolonged hospitalization. Nerve injury at the side of the operation allows detection of sensory loss and signs of sensitization from cutaneous and deep structures with quantitative sensory testing. This method demonstrated increased thresholds of sensory disturbances (tactile, warmth, cool, heat pain) in patients with and without thoracic pain (7).

Chronic pain after thoracic surgery, mainly thoracotomy, is a relatively well documented topic. However, there has been a notable gap in research concerning the incidence of early persistent pain (EPP), especially in the context of VATS, that is reported in the initial postoperative phase, 3 to 4 weeks after surgery, a period between the acute and chronic pain phase. Our experience indicates that EPP is relatively underappreciated and receives scant attention in the clinical setting. The primary objective of our study is to elucidate the incidence of EPP after VATS. Additionally, we evaluate risk factors that contribute to EPP and its characterization in the clinical setting. By being aware of EPP, clinicians can better inform patients about the expected pain trajectory, leading to improved patient care. This knowledge allows caregivers to anticipate the transition from acute to chronic pain, ultimately enhancing patient quality of life. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-802/rc).

Highlight box

Key findings

- The incidence of early persistent pain (EPP) at 3 to 4 weeks after video-assisted thoracoscopic surgery (VATS) was 16.2%, with acute pain being the most important risk factor.

What is known and what is new?

- After VATS, pain and discomfort were most frequently reported in the utility and ventral incisions, with a notable increase in involvement of the dorsal incision in patients with EPP. Additionally, hypoesthesia, hyperesthesia, and a positive pinch test were the predominant sensory abnormalities among all patients.
- The incidence of chronic pain and, acute pain being a significant risk factor, is well described in thoracic surgery, especially after thoracotomy.
- This study highlights the incidence of EPP, emphasizing its role in the postoperative pain cycle and the expected pain trajectory.

What is the implication, and what should change now?

- This knowledge allows caregivers to anticipate the transition from acute to chronic pain by understanding the incidence and clinical characteristics of EPP after VATS, ultimately enhancing patient quality of life.

Methods

Study design and patient selection

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This prospective observational cohort study was performed in a Dutch teaching hospital (Máxima Medical Center, Veldhoven) and approved by its Medical Ethical Committee (No. 2021-MMC-003). Patients were asked for informed consent to remain in follow-up and answer additional questionnaires. We included all consecutive patients who underwent VATS in our hospital (Maxima Medical Center) between 4th of January 2021 and 1st of March 2023. We excluded patients with conversion to open thoracotomy or not undergoing the intended VATS, with previous specialized treatment in a pain clinic due to severe pain, or who had additional surgery

the same day as the VATS procedure (since this may bias the presence of thoracic pain). Patients who occasionally utilized opioids were included in the study population. Patients who underwent a second VATS within at least 6 weeks after a first VATS procedure and did not suffer from pain after the first operation, remained in the analysis. If patients completed their postsurgical follow-up in another hospital (their reference hospital), clinically deteriorated or deceased after the VATS procedure, no follow-up data registration was obtained at 3 to 4 weeks after the procedure and were excluded. Six patients died related to severe acute postoperative complications. See the flow diagram in *Figure 1*.

Surgery and anaesthesia

All patients underwent VATS with uniportal (n=11) or multiportal technique [4-port technique according to McKenna (8); n=106]. A rib spread retractor was never used. Indications for a VATS procedure included: primary lung carcinoma, lung metastasis, diagnostic procedures (e.g., pleural biopsies), pneumothorax, thoracic empyema or hyperhidrosis. All patients received a postoperative chest tube.

All patients received general anaesthesia and were intubated. Due to an ongoing randomized trial, three different postoperative analgesic techniques were performed in our clinic according to the study protocol (9): thoracic epidural analgesia (TEA), continuous paravertebral block (PVB) or single-shot intercostal nerve block (ICNB). Some patients received a continuous ICNB with an infiltration catheter as described by Bousema *et al.* (10).

Data collection

Data was prospectively collected from electronic medical records into an electronic case report form. Pain was measured by the numerical rating scale (NRS) score at baseline (preoperatively), postoperatively at the recovery room once the patient was awake, at the evening of the surgery and 3 times per day at postoperative day (POD) 1 until 5 (or until discharge), as this is standard of care in our hospital (a maximum number of 17 postoperative NRS measurements per patient was possible). Patients routinely had a postoperative follow-up appointment at the surgical outpatient clinic 3 to 4 weeks after hospital discharge and were asked about the presence of pain. In addition, standard physical examination was performed to identify the location of the pain and to describe characteristics of neuropathic pain according to the Douleur Neuropathique 4 (DN4) (11) questionnaire: hypoesthesia (numbness), hyperesthesia (increased sensitivity), altered cool perception (abnormal response to a wet cotton fabric), positive pinch test (painful pinching of the skin compared to a painless pinch at the contralateral side) and a tender point (one specific location of tenderness or pain to palpation).

EPP was diagnosed if during follow-up at 3 to 4 weeks a NRS score ≥4 was noted, as this is a clinical threshold for identifying unacceptable pain requiring additional pain medication (12).

If EPP was present and accompanied by a DN4 score ≥4 (indicating neuropathic pain), patients were asked to answer additional questionnaires: DN4, the EORTC Core Quality of Life questionnaire (EORTC QLQ-C30), Hospital Anxiety and Depression Scale (HADS) and the McGill Pain Questionnaire (MPQ).

Definitions

Pain was defined as a NRS ≥4, and was considered acute when present during POD 0 until 5 (or until discharge) and as EPP when present at 3 to 4 weeks after VATS. Patients with acceptable pain (NRS <4) or no pain (NRS 0) at 3 to 4 weeks after surgery were defined as patients without EPP.

Primary and secondary outcomes

The primary outcome was the incidence of EPP. Secondary outcomes were (I) the assessment of risk factors for EPP; (II) characteristics during physical examination, reporting hypoesthesia, hyperesthesia, altered cool perception, positive pinch test and a tender point; (III) acute pain scores measured at POD 0 until 5 (or until discharge); (IV) the use of additional analgesia (postoperative opioid or non-opioid medication in addition to regional analgesia) after surgery from POD 0 until 5 [number of patients that required additional analgesia and the amount of opioids converted to opioid oral morphine milligram equivalent (MME)] (13); and (V) complications according to the Clavien-Dindo classification. No imputation for missing values was done for secondary outcomes.

Statistical analysis

Data analysis was performed with SPSS statistical software version 22 (SPSS Inc., Chicago, IL, USA). The incidence of EPP was expressed as a rate estimate with a 95% confidence interval (CI).

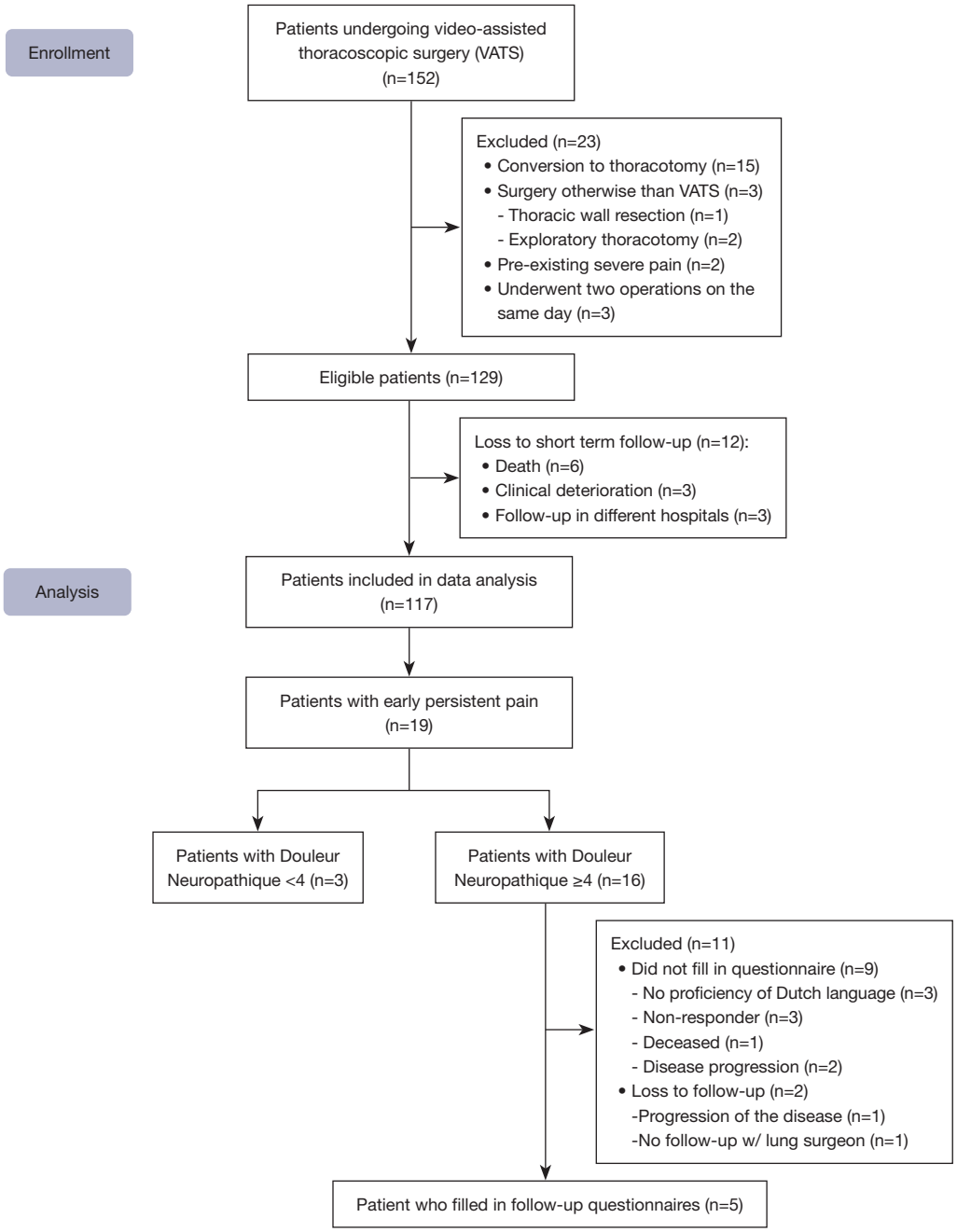

Figure 1 Patient selection process flow diagram. VATS, video-assisted thoracoscopic surgery.

To assess risk factors for EPP, univariate logistic regression was used to evaluate several known or theoretical risk factors (age, gender, history of a psychiatric disorder, type of operation and acute postoperative pain as % NRS ≥4). Variables with a P value <0.1 in the univariate model were then combined in a multivariate logistic regression model to assess their independent correlation. In addition, comparisons were made between patients with and without EPP using the unpaired *t*-test or Mann-Whitney *U* test for continuous variables or with Egon Pearson's N – 1 Chi-squared statistic for categorical variables. Distribution of continuous variables was assessed using the Shapiro-Wilk test and described as means with standard deviation (SD) when normally distributed, or with medians with

interquartile range (IQR) when non-normally distributed.

The NRS pain scores from POD 0 until 5 as a measure of acute pain were analysed as repeated measurements with a linear mixed model. A within-subject and a between-subject factor analysis was performed: measurement number, the incidence of EPP and the operation indication were used as fixed factors, while the type of operation was used a random factor (inter-object variability). The covariance structure with the lowest Akaike Information Criterion index was applied.

Since the aim of the study was descriptive and observational, no a priori sample size calculation was performed, aiming to include consecutive patients during 2 years. With the current sample size, we achieve a power of 98.75% (Appendix 1).

Results

A total of 152 unique patients underwent VATS between January 2021 and March 2023, of which 129 were eligible and 117 were complete cases for inclusion in the analysis (*Figure 1*). Median age was 64 years, 54.7% was male and 27.4% were smokers (*Table 1*). Types of surgery are shown in *Table 1*. The median length of stay (LOS) was 4 days (IQR, 3–6.5 days).

Primary outcome

The incidence of EPP (NRS ≥4) at 3 to 4 weeks' follow-up was 16.2% (n=19; 95% CI: 9–23%).

Secondary outcomes

Univariate logistic regression analysis demonstrated that male gender and absence of a psychiatric disorder had a lower likelihood of experiencing EPP than female gender and patients having a psychiatric disorder (*Table 2*). Furthermore, acute postoperative pain [% NRS ≥4; odds ratio 1.041 (95% CI: 1.020–1.062), P<0.001] showed a strong relationship with the presence of EPP. In a multivariate logistic regression analysis, only acute postoperative pain remained strongly associated to EPP (P≤0.001).

Details on the distribution of pain or discomfort at clinical examination are depicted in *Table 3* and *Figure 2*. In general, the utility and ventral incision were the most common locations of pain, whereas hypoesthesia, hyperesthesia and positive pinch test were the most common sensory abnormalities.

Pain at the utility (P<0.001) and dorsal (P=0.02) incision as well as the presence of hyperesthesia (P=0.01), altered cold perception (P=0.008) and a tender point (P=0.004), were significantly more present in patients with EPP than in patients without EPP (*Table 3* and *Figure 2*).

Per patient, the mean number of NRS measurements during hospitalization was 7 (SD 3). A linear mixed model of acute postoperative pain scores showed significant differences between patients who did and did not develop EPP, with higher pain scores during all measurements for the EPP during the acute postoperative phase (*Figure 3*). Only on POD 5, pain scores were not significantly different anymore (*Table 4*). When asking at follow-up, patients without EPP were satisfied with their type of postoperative analgesia in 91.2% of the time, while this was 60.0% in patients with EPP (P=0.02).

Of the patients experiencing EPP accompanied by a DN4 score ≥4, 5 of the 16 patients completely filled in the questionnaires (*Figure 1*) at 3 to 4 weeks. The EORTC QLQ-C30 questionnaire demonstrated functional impairment and reduced quality of life through decreased physical, role, emotional, cognitive and social functioning as well as symptoms of fatigue, pain, dyspnoea, insomnia (Appendix 2). The HADS was >8 indicating considerable symptoms of anxiety or depression in 2 patients (Appendix 2). The MPQ showed that all patients developed pain postoperatively, acutely or gradually, it mostly also referred to other locations and changed in intensity but was never gone. The description of pain was variable and mostly included the terms: annoying, burning, nagging, tight, tiring, stinging, drilling and itchy.

The number of patients using paracetamol and non-steroidal anti-inflammatory drugs as well as the amount of opioid oral MME were equal in both groups from POD 0 until 5 (*Table 5*). However, compared to patients without EPP, the number of patients using oral and intravenous opioids was significantly higher in patients with EPP at the recovery room (P=0.001) and on POD 2 (P=0.003).

The complication rates did not differ between patients with or without EPP (P=0.50) (*Table 5*). Also, no differences were observed in rates of re-operations by VATS (P>0.99) and admission at the ICU (P=0.67) (*Table 1*).

Discussion

The present analysis revealed that 16.2% (95% CI: 9–23%) of patients reported EPP at postoperative follow-up after

Table 1 Patient characteristics

Characteristics	All patients (n=117)	Patients with EPP (n=19)	Patients without EPP (n=98)	P value
Patient characteristics				
Age (years), median [IQR]	64 [53–72]	64 [56–73]	57 [52–71]	0.47
Gender (male), n (%)	64 (54.7)	7 (36.8)	57 (58.2)	0.09
BMI (kg/m^2), mean (SD)	26.0 (5.6)	27.0 (4.8)	25.8 (5.8)	0.42
Smoking status*, n (%)				0.08
Smoker	32 (27.4)	9 (47.4)	23 (24.2)	
Non-smoker	19 (16.2)	1 (5.3)	18 (18.9)	
Ex-smoker**	63 (53.8)	9 (47.4)	54 (56.8)	
Medical history, n (%)				
Thorax surgery in the past	48 (41.0)	7 (50.0)	41 (51.9)	0.56
Pain syndromes	3 (2.9)	2 (14.3)	1 (1.3)	0.06
Psychiatric disorder	17 (14.5)	6 (40.0)	11 (17.7)	0.08
Pre-operative NRS ≥4*, n (%)	2 (1.7)	1 (5.6)	1 (1.1)	0.30
Surgical characteristics				
Type of surgery, n (%)				0.83
Anatomical resection	67 (57.3)	12 (63.2)	55 (56.1)	
Wedge resection	18 (15.4)	3 (15.8)	15 (15.3)	
Evacuation empyema/hematoma	8 (6.8)	0	8 (8.2)	
Pleurodesis	16 (13.7)	3 (15.8)	13 (13.3)	
Biopsy lung or pleura	6 (5.1)	1 (5.3)	5 (5.1)	
Sympathectomy	2 (1.7)	0	2 (2.0)	
Surgical technique, n (%)				
Multi-port VATS***	106 (90.6)	18 (94.7)	88 (89.8)	0.69
Uni-port VATS	11 (9.4)	1 (5.3)	10 (10.2)	0.69
Operation time (minutes), mean (SD)	111.9 (56.6)	113.1 (60.6)	111.6 (56.1)	0.92
One chest tube, n (%)	107 (91.5)	18 (100.0)	89 (91.8)	0.45
Re-VATS, n (%)	6 (5.1)	1 (5.3)	5 (5.2)	>0.99
Admission intensive care, n (%)	10 (8.5)	2 (10.5)	8 (8.2)	0.67
Analgesic characteristics				
Postoperative analgesic technique, n (%)				0.81
Thoracic epidural analgesia	38 (32.5)	6 (31.6)	32 (32.7)	
Paravertebral block	32 (27.4)	5 (26.3)	27 (27.6)	
Intercostal nerve block$^+$	43 (36.7)	8 (42.1)	35 (35.7)	
Only opioids	4 (3.4)	0	4 (4.1)	
Duration of continuous locoregional analgesia (days), mean (SD)	1.80 (1.05)	1.92 (1.00)	1.77 (1.04)	0.63

*, not all data were complete per characteristic, missing values are not presented in the table and hence denominators can slightly differ; **, ex-smoker: stopped smoking at least 1 month ago; ***, multi-port VATS utilizes either 2 or 3 ports; $^+$, intercostal nerve block given as single shot or with a continuous infiltration catheter. EPP, early persistent pain; IQR, interquartile range; BMI, body mass index; SD, standard deviation; NRS, numerical rating scale; VATS, video-assisted thoracoscopic surgery.

Table 2 Multivariate regression analysis

Variables	Coefficient (B)	OR	95% CI	P value
Univariate regression analysis				
Age (years)	−0.003	0.997	0.964–1.031	0.86
Gender (male)	−0.868	0.420	0.152–1.158	0.09
Psychiatric disorder (absence)	−1.295	0.274	0.086–0.868	0.03
Type of surgery*	−0.248	0.781	0.431–1.415	0.42
Acute postoperative pain**	0.040	1.041	1.020–1.062	<0.001
Multivariate regression analysis				
Gender (male)	−0.125	0.883	0.269–2.897	0.84
Psychiatric disorder (absence)	−1.277	0.279	0.073–1.066	0.06
Acute postoperative pain	0.038	1.039	1.017–1.062	<0.001

*, as described in the table referring to patient characteristics; **, acute postoperative pain was analyzed as percentage of all registered NRS scores that were ≥4 (as continuous measure). OR, odd ratio; CI, confidence interval; NRS, numerical rating scale.

Table 3 Location of pain and characteristics of sensory abnormalities after video assisted thoracoscopic surgery (all patients and a comparison between patients with and without early persistent pain)

Variables	All patients (n=117)	Patients with EPP[#1] (n=19)	Patients without EPP[#2] (n=98)	P value
Location				
Caudal incision	3 (2.9)	1 (5.6)	2 (2.4)	0.44
Utility incision	20 (19.4)	12 (66.7)	8 (9.4)	<0.001
Ventral incision/chest tube	23 (22.3)	7 (38.9)	16 (18.8)	0.07
Dorsal incision	7 (6.8)	4 (22.2)	3 (3.5)	0.02
General thorax	2 (1.9)	1 (5.6)	1 (1.1)	0.31
Characteristic				
Hypo/dysesthesia	17 (16.3)	3 (16.7)	14 (16.3)	0.60
Hyperesthesia	22 (21.2)	8 (44.4)	14 (16.3)	0.01
Altered cold perception	6 (5.8)	4 (22.2)	2 (2.3)	0.008
Pinch test positive	22 (21.4)	6 (33.3)	16 (18.8)	0.15
Tender point	8 (7.8)	5 (27.8)	3 (3.5)	0.004
Intervention	2 (1.9)	1 (5.6)	1 (1.1)	0.31

All data are expressed as number of patients (n) and percentage (%). [#1], patients with unacceptable pain (NRS ≥4); [#2], patients with no/acceptable pain (NRS <4). EPP, early persistent pain; NRS, numerical rating scale.

3 to 4 weeks. Through multiple regression analysis, we identified acute postoperative pain as the most relevant risk factor associated with EPP. Pain and discomfort were most frequently reported in the utility and ventral incisions, with a notable increase in involvement of the dorsal incision in patients with EPP. Additionally, hypo- and hyperesthesia, as well as a positive pinch test, were the predominant sensory abnormalities among all patients. Patients with EPP exhibited higher pain scores during the acute postoperative phase until POD 4, and more patients relied on oral and intravenous opioids until POD 2. Despite these remarkable differences in acute pain between patients with or without

EPP, no difference was measured in LOS and complications.

The literature recognizes that a higher incidence of acute pain after VATS is an important factor associated with chronic pain, and our study further unveils its association with EPP. Postoperative pain after thoracic surgeries mostly focuses on thoracotomy procedures, underestimating the incidence and severity of pain after VATS (14). Acute pain after VATS is not rare and is attributed to surgical etiologies including mechanical forces, neural stretch or compression and unrecognized nerve transection (15). In the present study, patients with EPP had significantly higher acute pain scores compared to patients without EPP at POD 0 until 4. In a retrospective study by Ross *et al.* (16), patients with chronic pain were found to have higher levels of acute pain in the first 24 hours postoperatively and the last 24 hours of admission before discharge from the hospital. A similar trend was seen by (7), in which patients with chronic pain had higher mean pain scores at POD 1 than patients without chronic pain and at POD 7 this difference persisted. It is imperative to prioritize optimal postoperative analgesia

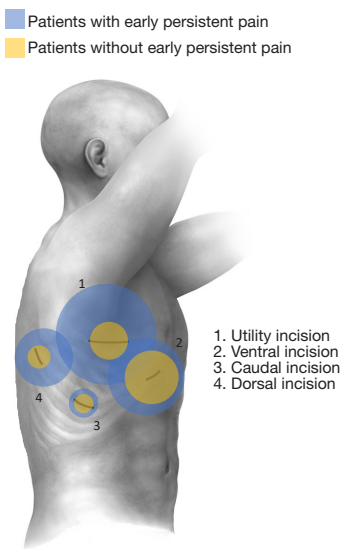

Figure 2 Visualization of the proportion of patients with discomfort (NRS <4) or pain (NRS ≥4) at the incisional locations of video-assisted thoracoscopic surgery as described in *Table 1*. NRS, numeric rating scale.

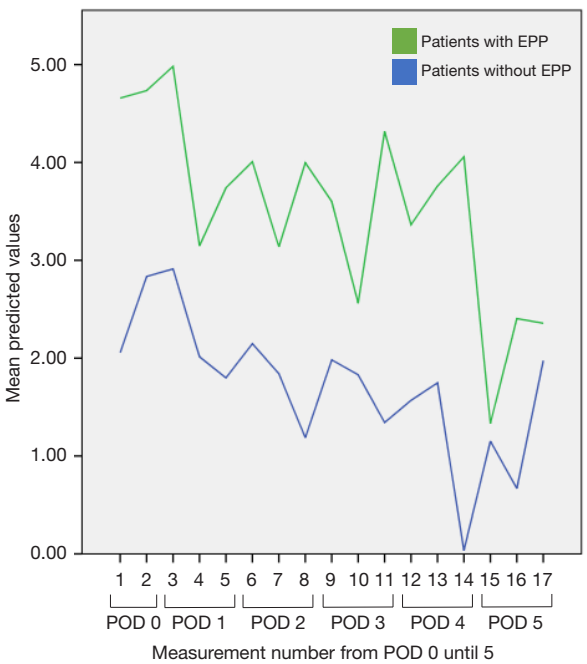

Figure 3 Linear mixed model of repeated pain score measurements from POD 0 until 5 for patients with and without early persistent pain. EPP, early persistent pain; POD, postoperative day.

Table 4 Mean pain scores with standard deviations during postoperative day 0 until 5 for patients with and without early persistent pain

Variables	Patients with EPP		Patients without EPP		Mean difference	P value
	n	Score, mean (SD)	n	Score, mean (SD)		
Day of surgery	18	4.31 (2.82)	91	2.35 (2.00)	−1.95	0.01
Postoperative day 1	17	3.86 (2.10)	95	2.20 (1.75)	−1.66	0.001
Postoperative day 2	19	3.61 (1.85)	87	2.09 (1.65)	−1.52	0.001
Postoperative day 3	14	3.38 (1.67)	70	1.88 (1.91)	−1.50	0.007
Postoperative day 4	12	3.35 (2.23)	48	1.66 (1.68)	−1.69	0.005
Postoperative day 5	6	2.31 (1.49)	28	1.35 (1.57)	−0.96	0.18

EPP, early persistent pain; n, sample size; SD, standard deviation.

Table 5 Additional analgesia and complications

Type of analgesia per day	Patients with EPP		Patients without EPP		P value
	n	Value (n=19)	n	Value (n=98)	
Recovery room					
Paracetamol, n [%]	19	12 [63]	98	65 [66]	0.49
NSAIDs, n [%]	19	2 [11]	98	12 [12]	0.60
Opioids, n [%]	19	14 [74]	98	33 [34]	0.001
MME, mean [SD]	13	16 [12]	30	15 [8]	0.70
Postoperative day 1					
Paracetamol, n [%]	19	19 [100]	98	87 [89]	0.21
NSAIDs, n [%]	19	8 [42]	98	45 [46]	0.76
Opioids, n [%]	19	12 [63]	98	40 [41]	0.07
MME, mean [SD]	12	36 [26]	40	35 [43]	0.97
Postoperative day 2					
Paracetamol, n [%]	19	15 [79]	96	78 [81]	0.76
NSAIDs, n [%]	19	8 [42]	96	54 [56]	0.26
Opioids, n [%]	19	14 [74]	96	35 [37]	0.003
MME, mean [SD]	14	42 [44]	35	30 [34]	0.30
Postoperative day 3					
Paracetamol, n [%]	15	15 [100]	77	59 [77]	0.04
NSAIDs, n [%]	15	4 [27]	77	29 [38]	0.42
Opioids, n [%]	15	9 [60]	77	31 [40]	0.16
MME, mean [SD]	9	30 [24]	31	28 [38]	0.92
Postoperative day 4					
Paracetamol, n [%]	12	8 [67]	56	40 [69]	>0.99
NSAIDs, n [%]	12	3 [25]	56	21 [38]	0.52
Oral opioids, n [%]	12	5 [42]	56	17 [30]	0.51
MME, mean [SD]	5	31 [17]	17	33 [30]	0.89
Postoperative day 5					
Paracetamol, n [%]	8	6 [75]	36	26 [72]	>0.99
NSAIDs, n [%]	8	1 [13]	36	12 [33]	0.40
Opioids, n [%]	8	3 [38]	36	8 [22]	0.39
MME, mean [SD]	3	34 [4]	8	28 [21]	0.66
Complications, n [%]	–	2 [10.5]	–	16 [16.3]	0.50
Clavien-Dindo 1–2	–	2 [100]	–	9 [56.3]	
Clavien-Dindo 3–4	–	0	–	7 [43.8]	

EPP, early persistent pain; NSAIDs, non-steroidal anti-inflammatory drugs; MME, morphine milligram equivalents; SD, standard deviation.

to decrease the risk of EPP and increase patient satisfaction, especially in patients with acute postoperative pain during hospitalization until discharge, as the probability of developing EPP and chronic pain is higher. Loco-regional analgesic techniques are recommended (17), as supported by a multidisciplinary working group of pain experts (18). Health care workers are encouraged to actively ask about pain during these first few days and intervene even before discharge from the hospital.

By extensive clinical examination of all participating patients, we studied the presence of sensory abnormalities after VATS and found that both patients with and without EPP presented with sensory disturbances. The most common included hypoesthesia, hyperesthesia and a positive pinch test. The International Association for the Study of Pain (IASP) defines these terms, respectively, as decreased and increased sensitivity to stimulation and an unpleasant feeling when pinched at the area of discomfort. A large cross-sectional survey on chronic pain performed in Norway among 12,982 patients, showed a strong association between sensory abnormalities and persistent pain, increasing with higher pain intensities (19). In our study, all patients with EPP did have at least one sensory disturbance, mostly hyperesthesia, confirming the presence of a neuropathic component. A study by Steegers *et al.* (20), in a population who underwent VATS and developed chronic pain, 23% of the patients had definite neuropathic pain, 30% possible and 47% definitely did not have neuropathic pain. Wildgaard *et al.* (7) performed a long-term neurophysiological characterization of postoperative pain syndromes in patients after thoracic surgery and suggested nerve injury to be present in both patients with and without chronic pain. Also, hypoesthesia and hyperesthesia were present in both groups, with no statistical differences found. However, this initial (maybe unavoidable) nerve damage during VATS is the initiator of a cascade of biological events resulting in nociceptive pain (caused by incision) and inflammatory pain (due to inflammatory mediators) which persist until the wound is healed and finally, neuropathic pain (due to persistent nerve injury and hypersensitivity) (21). Proactively asking about sensory abnormalities and performing a physical examination, with the DN4 questionnaire as a guidance tool, can be instrumental in diagnosing the early presence of neuropathic features of pain. To conclude, sensory abnormalities suggesting nerve damage may be present in patients with and without pain complaints, predominantly hyperesthesia and hypoesthesia, resulting from a known and complex cascade of nociceptive, inflammatory and central nervous system pain stimulators.

These findings highlight the importance of optimal acute pain management through a multidisciplinary approach, to reduce the risk of EPP and later developing chronic pain. In a published meta-analysis, estimates of the incidence of chronic pain after VATS in the literature vary widely as a consequence of different definitions, postoperative follow-up and small sample sizes of published studies (22). In our study, only one patient of the selected group experiencing EPP (n=19) developed chronic pain at 3 and 6 months after surgery. The presence of acute pain can be ameliorated through reducing surgical trauma, applying multimodal analgesia protocols including perioperative loco-regional analgesia techniques and postoperative protocols enhancing mobilization, the use of digital chest tube systems, lung physiotherapy and individual patient care when acute pain is not eradicated before discharge from the hospital (23).

Strengths and limitations

Although we included consecutive patients undergoing VATS in a prospective and standardized clinical setting over a 2-year period, the small amount of patients developing EPP (according to our definition) precludes strong statistical conclusions. Also, the diverse background has to be taken into consideration. However, this prospective longitudinal cohort study enhanced standardized postoperative care for all VATS patients in our hospital, giving a realistic exposure of the incidence of EPP and the importance of optimal management of acute postoperative pain to reduce the risk of both EPP and chronic pain. It is important to consider that a different definition can have implications for the incidence found.

Conclusions

The incidence of EPP at 3 to 4 weeks after VATS was 16.2% (95% CI: 9–23%). Acute postoperative pain is the most relevant risk factor for developing such EPP. Optimal early postoperative analgesia with a multimodal approach may be key to reduce acute postoperative pain and its subsequent risk for EPP. The latter appeared to be significantly more frequently associated with specific sensory abnormalities such as hyperesthesia, an altered cold perception and a tender point, suggesting neuropathic pain

due to nerve injury.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-802/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Maxima Medical Center Medical Ethical Committee (No. 2021-MMC-003) and informed consent was taken from all the patients when additional follow-up was applicable. All data is anonymized and cannot be traced back to individuals.

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