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Original Research Article

ACUTE & PERIOPERATIVE PAIN SECTION

Preoperative Patient Expectations of Postoperative Pain Are Associated with Moderate to Severe Acute Pain After VATS

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Abstract

Objective. The goal of this *post hoc* analysis of subjects from a prospective observational study was to identify the predictors of patients developing moderate to severe acute pain (mean numerical rating scale [NRS] $\geq$4, 0–10) during the first three days after video-assisted thoracoscopic surgery (VATS) from a comprehensive evaluation of demographic, psychosocial, and surgical factors. **Methods.** Results from 82 patients who were enrolled one week before VATS and evaluated during the first three postoperative days are presented. The primary outcome variable of the current study was the presence of moderate to severe acute pain after VATS. **Results.** Fifty-nine percent (95% confidence interval, 47–69%) of study subjects developed moderate to severe acute pain after VATS. Factors univariately associated with the presence of moderate to severe acute pain were greater average expected postoperative pain, greater pain to a suprathreshold cold stimulus, and longer durations of surgery and hospital stay ($P < 0.05$). When considered in the multiple logistic regression models, the patients' preoperative average intensity of expected postoperative pain (NRS, 0–10) was the only measure associated with the moderate to severe acute pain. Average intensity of postoperative pain expected by patients when questioned preoperatively mediated the effect of reported intensity of pain to the suprathreshold cold stimulus for moderate to severe acute pain levels. Preoperative patient expectations had greater predictive value than other assessed variables including psychosocial factors such as catastrophizing or anxiety assessed one week before surgery. **Conclusions.** None of the preoperative psychosocial measures were associated with the moderate to severe acute pain after VATS. Average expected postoperative pain was the only measure associated with the development of moderate to severe acute pain after VATS.

Key Words: Acute Pain; Thoracic Surgery; VATS; Predictors; Multiple Logistic Regression

Introduction

In the United States, more than 40,000 thoracic surgeries are performed each year. Most are performed to treat lung cancer or infection [1]. Thoracic surgery can involve either open thoracotomy or the less invasive video-assisted thoracoscopic surgery (VATS; or thoracoscopy). VATS procedures are increasing [2,3] and continue to gain popularity [4–7]. Even though VATS is less invasive than open thoracotomy, moderate to severe acute pain remains common after VATS [8], and it is associated with significant rates of chronic pain [8–11].

Previous studies on other operations such as surgery for breast cancer and cesarean delivery have suggested that preoperative psychological factors, pain perception, quantitative sensory testing (QST), preexisting chronic pain, or expected postoperative pain are associated with acute postoperative pain severity [12–16].

The goal of this study was to detect the predictors of developing moderate to severe acute pain after VATS from a comprehensive preoperative evaluation of demographic, psychosocial, and surgical factors. Our hypothesis was that developing moderate to severe acute pain following VATS is not only associated with surgical- and anesthesia-related factors, but also preoperative psychosocial measures. We previously reported predictors of chronic pain at six months after both thoracotomy and VATS for this data set and noted that acute postoperative pain was the only predictor of chronic pain after thoracic surgery [9]. In the current study, predictors of acute postoperative pain for VATS patients are assessed. The primary outcome variable for the current study was the presence of mild vs moderate to severe average acute pain intensity over the first three postoperative days.

Methods

This prospective, observational cohort study was approved by the University of Iowa (Iowa City, Iowa) Institutional Review Board (201202796). The STROBE reporting guidelines for observational studies were followed [17]. VATS patients were recruited from the University of Iowa Hospitals and Clinics (UIHC; N = 71) and the Iowa City Veterans Affairs Medical Center (VAMC; N = 11), both located in Iowa City, Iowa. The Iowa City VAMC's thoracic surgery clinic was staffed by the University of Iowa Thoracic Surgery Clinic, and patient care was similar. Patients were approached for consent during their preoperative visit approximately one week before their VATS.

Details regarding trial design are described elsewhere [9]. In brief, to be eligible, patients must have spoken English, been 18 to 80 years old, and been scheduled for VATS. The surgical procedures included VATS with excision-plication of bullae, with lobectomy, with partial or total pulmonary decortication, or with wedge resection of lung. Patients with limitations of self-expression or visual dysfunction or having emergency surgery, a severe psychiatric illness, or chronic pain problems in the chest area for longer than two months before VATS were excluded. Pregnant women and prisoners were also excluded.

Data from 99 patients, who were enrolled between March 8, 2013, and December 21, 2015, were previously presented for the analysis of chronic pain at six months after thoracic surgery (thoracotomy and VATS) [9]. Toward the end of that study, in addition to other evaluations, we added an optional component to the study, and enrollment was continued until July 19, 2016. Sixty-nine patients presented in the current study were also evaluated in the previous study [9]. Thoracotomy patients were excluded from this acute pain analysis.

Preoperative Psychosocial Assessment

As reported previously [9], following informed consent, patients were asked to complete five computer-adaptive PROMIS [18] questionnaires for anxiety, depression, physical role function, fatigue, and sleep disturbance. These computer-adaptive questionnaires contain a large collection of items measuring one characteristic; each subsequent question is chosen depending on the patient's responses to previous queries, thus limiting the number of questions. The results of the PROMIS questionnaires are presented as standardized T-scores with a mean of 50 and a standard deviation of 10. Therefore, a patient with a physical function T-score of 40 is 1 SD below the US general population mean [19]. Patients then completed three additional questionnaires examining 1) post-traumatic stress disorder (PCL-C [20]), 2) catastrophizing (Pain Catastrophizing Scale [PCS] [21]), and 3) psychological acceptance (AAQ-II [22]).

Preoperative Pain Assessment

During the preoperative visit, patients were asked to rate their current pain at rest using the NRS (0–10): "Please rate your current pain at rest by indicating the number that best describes your pain where 0 means no pain and 10 is the worst imaginable pain." Next, we asked patients to cough strongly two times and rate their pain with coughing (NRS, 0–10, "Please rate your current pain during coughing"). They were asked to rate their expected postoperative pain severity for each of their first three postoperative days (PODs). We used an NRS (0–10) and asked, "Please rate your expected average pain on each of the three first postoperative days." We calculated the mean of the expected postoperative pain severity scores from the first three PODs as the average expected postoperative pain.

Patients' gender and history of tobacco and alcohol use were also asked at this preoperative visit.

Quantitative Sensory Testing

As described previously [9], the preoperative pain threshold to cold test was measured using the Thermal Sensory Analyzer-II (Medoc Inc., Israel) via 30 × 30 mm contact thermode. The probe was applied to the forearm using a starting temperature of 30°C (86°F), and the temperature was decreased by 1°C/s (1.8°F/s) increments until the patient experienced pain. The patient was asked to click a button when the nonpainful cold sensation changed to a painful sensation, and the temperature of the probe was returned to 30°C (86°F). If the patient did not stop the test, the lowest temperature reached was 10°C (50°F), and the temperature returned to 30°C (86°F). This process was repeated three times, and the average of three measurements (°C) was the pain threshold to cold.

To estimate pain intensity to the suprathreshold cold stimulus, the thermal testing device cooled to 10°C (50°F) and was held at that temperature for 15 seconds.

At the end of the 15 seconds, patients were asked to rate their pain using the NRS (0–10). This process was repeated three times, and the average of three measurements (NRS) was the pain to the suprathreshold cold stimulus.

Surgery, Anesthesia, and Pain Management

The type of surgery was determined by the surgeon as their usual care. Intraoperative management was determined by the anesthesiologist. Postoperatively, patients undergoing VATS received patient-controlled analgesia using hydromorphone, morphine, or fentanyl ($N = 1$) until they tolerated oral nutrition and oral pain medications. In 11 patients, the surgeons requested epidural analgesia preoperatively, anticipating progressing to open thoracotomy; however, the patients underwent VATS without progressing to thoracotomy. Thus, 11 VATS patients received thoracic epidural analgesia, as described earlier [9]. We recognize that this may modify immediate postoperative pain but chose to analyze all VATS patients.

First Three Postoperative Days

Research assistants visited patients daily during the first three PODs to collect the average pain intensity (NRS, 0–10). We asked patients to "Please rate your pain on average in the last 24 hours." From the mean of these three daily NRS values, the average postoperative pain score was derived. A chest tube was counted as present if the patient had a chest tube at 6:00 AM that day. When patients were discharged before POD 3 or during the weekend, the data collection form to measure the severity of pain was given to the patient with a stamped return envelope.

Electronic Medical Records

Age, American Society of Anesthesiologists physical status, duration and type of surgery, number of ports, and postoperative analgesic use in terms of oral morphine equivalents from the time the subject arrived in the postoperative care unit until POD 3 were obtained from the patients' electronic medical records. Average daily opioid consumption was calculated by dividing the total postoperative analgesic use up to three PODs by the duration of hospital stay. For example, if a patient was discharged at the end of POD 2, the average of opioid consumption from POD 0, POD 1, and POD 2 was calculated. No further measurements were made after POD 3. In addition, whether patients were prescribed opioids at the time of their last preoperative clinic visit, preoperative radiation and/or chemotherapy within six weeks of surgery, and epidural usage for 11 patients starting the day of surgery up to three PODs were also obtained from the electronic medical records.

Statistical Analyses

If the average postoperative pain score was 4 or greater ($NRS \geq 4$, 0–10), then this was considered moderate to severe acute pain; otherwise it was classified as mild acute pain [23]. The primary outcome variable of the current study is the presence of mild vs moderate to severe (binary) acute pain over the first three postoperative days after VATS.

The two-sided 95% confidence interval (CI) for the incidence of moderate to severe acute pain was calculated according to Clopper and Pearson [24].

The normality of the continuous data was tested by the Shapiro-Wilk test and by examining the quantile-quantile plot. Normally distributed continuous variables were presented as mean ± SD and compared between the mild vs moderate to severe acute pain groups using a two-sample Student *t* test. When the distribution was not normal, the median along with first (Q_{25}) and third quartiles (Q_{75}) were presented, and a Wilcoxon rank-sum test was used. Categorical data were presented as frequency and percentage and were statistically tested using the chi-square or Fisher's exact test.

Multiple Logistic Regression Model

Those covariates with univariate P values < 0.10 were examined in the multiple logistic regression model for their association with the outcome of presence of mild vs moderate to severe acute pain. The covariates considered for the multiple regression model were gender, average expected postoperative pain, pain to the suprathreshold cold stimulus, presence of a chest tube on POD 1, and durations of surgery and hospital stay.

Backward model selection was performed to find the most parsimonious model based on the Akaike Information Criterion (AIC) [25]. To minimize the type I error rate, instead of $P < 0.05$, those covariates with $P < 0.01$ were included in the final multiple logistic regression model. Zhang and Yu recommended using relative risk instead of odds ratio when the incidence of an outcome of interest is $> 20\%$ [26]. To calculate the relative risk and associated 99% CI for key covariates for the final multiple regression model, the modified Poisson regression approach was used [27–29]. The goodness of fit of the final logistic regression model was evaluated by the Hosmer-Lemeshow test [30], where $P < 0.05$ indicates lack of fit. The area under the receiver operating characteristic curve (C-statistic) was also provided.

Note that, even though patients were enrolled from two different centers (UIHC and VAMC), the same surgeons operated on both groups of patients, and the patient care was similar. Therefore, center effect was not included in the multiple logistic regression model.

Correlation

The strength of the relationship between two continuous variables was assessed with Spearman's rank correlation

coefficients. The size of the correlation coefficients can be interpreted as low, moderate, high, and very high when the coefficient is in the range of 0.3–0.5, 0.5–0.7, 0.7–0.9, and 0.9–1.0, respectively [31].

Mediation Analyses

The mediating effect of average expected postoperative pain between the pain to the suprathreshold cold stimulus and moderate to severe acute pain was examined by assessing the direct and indirect effects. The mediating effect of average expected postoperative pain was concluded when all three of the following conditions were satisfied: 1) Pain to the suprathreshold cold stimulus significantly affects average expected postoperative pain (coefficient a is significant). 2) When the outcome is moderate to severe acute pain, in the presence of pain to suprathreshold cold, the effect of average expected postoperative pain is significant (coefficient b is significant). 3) The indirect effect (the product axb) is significant [32]. Bias-corrected bootstrap CIs for the indirect effects were calculated with 10,000 bootstrap samples [33]. The amount of mediation was quantified as percent mediated [34]. Mediation analyses were performed with the PROCESS macro in SAS for a binary outcome variable [33].

Sample Size Calculation

The sample size of the study was determined based on the logistical challenges, instead of a priori power calculations. The main goal of the parent study [9] was to collect complete six-month outcome data from 100 thoracotomy and VATS patients as preliminary data for a future larger study. Data from 82 VATS patients were included for this secondary analysis of acute pain.

Statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA). Plots were created using R, version 3.2.5 [35].

Results

Between March 8, 2013, and July 19, 2016, 504 patients were screened. From these, 107 patients scheduled for VATS were consented, and 93 patients were assessed during the first three PODs. One patient was sedated; pain scores were not obtained. Ten patients converted from VATS to thoracotomy and were excluded (Figure 1). Data from 82 VATS patients were presented. Two surgeons (KP and JK) performed 79% (65/82) of the operations. Patients were 61 ± 11 years old, and 46% (N = 38) were female.

Acute Pain

The mean of the average postoperative pain scores during the first three PODs was 4.4 ± 2.0 (N = 82). The average postoperative pain scores were 2.5 ± 0.9 for 41% of the patients (34/82) who were categorized in the mild pain group (NRS < 4) vs 5.7 ± 1.4 for those 59% (48/82, 95% CI = 47% to 69%) who were categorized in the moderate to severe (NRS ≥ 4) pain group. The distributions of the NRS values during each of the first three PODs, as well as the average postoperative pain scores, are presented in Figure 2.

Preoperative Evaluations

VATS patients with moderate to severe acute pain were more common among those with greater pain to the suprathreshold cold stimulus ($P = 0.03$) but not to cold pain threshold ($P = 0.33$) (Table 1). Patients with moderate to severe average postoperative pain scores had greater expected postoperative pain during each of the three PODs ($P < 0.03$ for each), as well as greater average expected postoperative pain ($P = 0.005$) than those with mild average pain scores. The remaining preoperative factors were not significantly different.

Preoperative Psychological Measurements

Results from the preoperative physical function score or the acceptance and action questionnaire indicated some trends. However, when the type I error rate of 0.05 was used, none of the preoperative psychosocial evaluations indicated a difference in those subjects with mild vs moderate to severe acute pain (Table 2).

Early Postoperative Evaluations

Most of the patients had lobectomy (39%) or wedge resection (61%). Median time to discharge was two days; 77% of the patients were discharged within three days (Table 3). Results for the presence of any chest tube are shown in Table 3. Most patients had only one chest tube. Four patients had more than one chest tube on POD 1. There were only two patients on POD 2 and one patient on POD 3 with more than one chest tube.

Among the anesthesia- and surgery-related factors that were considered, longer duration of surgery ($P = 0.026$) and hospital stay ($P = 0.04$) were the only factors univariately associated with having moderate to severe acute pain. Epidural use did not influence the number of patients with moderate to severe acute pain; 73% of the patients with epidural analgesia had moderate to severe acute pain vs 56% of the patients with no epidural use ($P = 0.35$).

Multiple Logistic Regression Model

According to the multiple logistic regression model (Table 4) after model selection, the only factor associated with moderate to severe acute pain was the average intensity of expected postoperative pain obtained during the preoperative assessment ($P < 0.01$). Patients with greater expected postoperative pain had a greater likelihood of developing moderate to severe acute pain (Figure 3). For example, those patients with an average expected postoperative pain score of 6 (NRS, 0–10) had

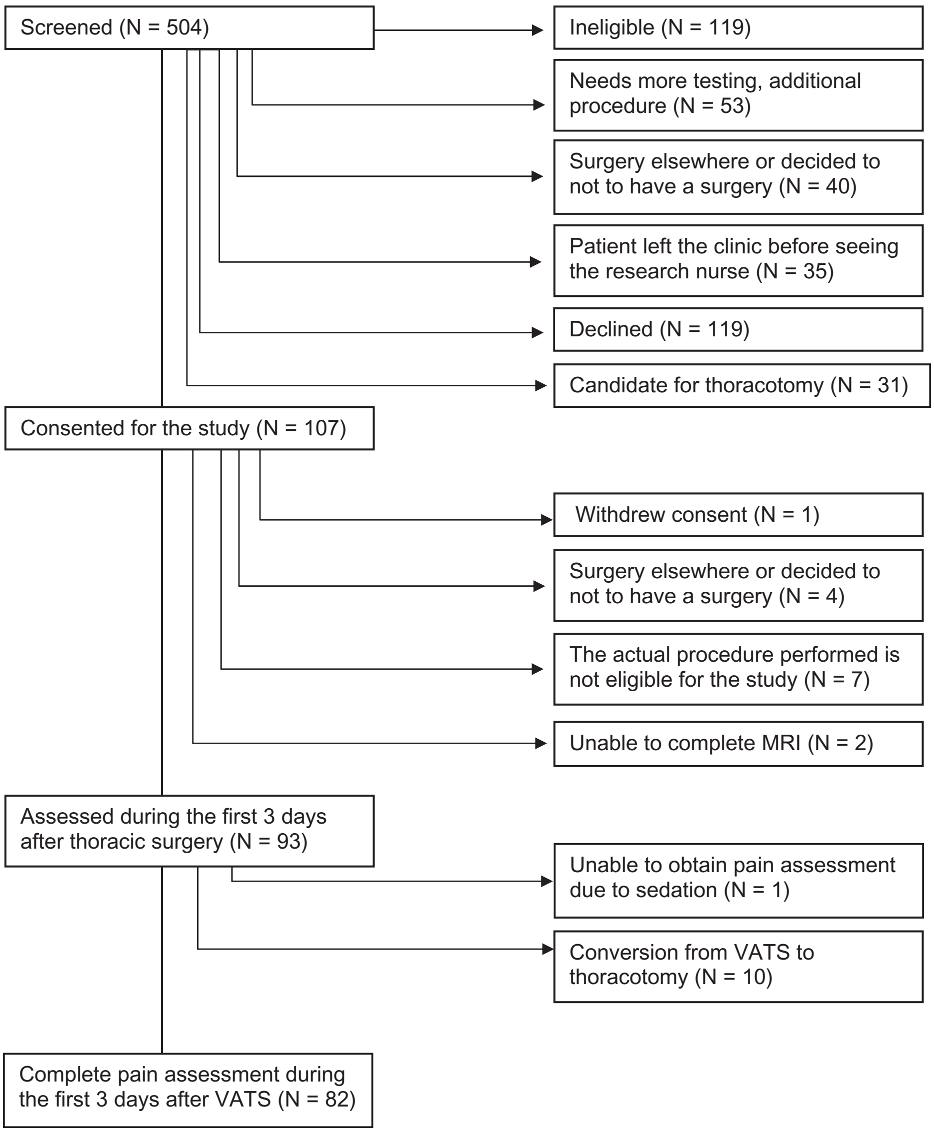

Figure 1. Flowchart of patients. MRI = magnetic resonance imaging; VATS = video-assisted thoracoscopic surgery.

a 2.0 times greater (95% CI = 1.1 to 3.5) chance of developing moderate to severe acute pain compared with patients with an average expected postoperative pain score of 4. The observed and expected pain ratings were weak to moderately correlated ($r = 0.43$, $P < 0.0001$).

The Hosmer-Lemeshow test indicated the model's adequacy ($P = 0.43$). The area under the curve (C-statistic) of the logistic regression model is 0.69, indicating that it did a fair job of discriminating between those with vs without moderate to severe acute postoperative pain.

Mediation Analyses

As presented in the *Results* section, when the type I error rate of 0.05 was used, only the average expected postoperative pain, pain to the suprathreshold cold stimulus, and durations of surgery and hospital stay were univariately associated with moderate to severe acute pain ($P < 0.05$). We wanted to assess the mediating effect of expected pain. By definition, mediator should occur temporally after the exposure [32]. Patients provided the expected intensity of postoperative pain (the potential mediator) before the duration of surgery and hospital stay were measured. Therefore, only the mediating effect of expected postoperative pain between the pain to the suprathreshold cold stimulus and moderate to severe acute pain was assessed.

Those patients with greater pain to the suprathreshold cold stimulus tended to have greater average expected postoperative pain (a = 0.23, 95% CI = 0.013 to 0.45, Spearman correlation $r = 0.20$, $P = 0.035$). When both pain to the suprathreshold cold stimulus and expected postoperative pain were in the multiple logistic regression model, expected postoperative pain remained significantly associated with moderate to severe acute pain. For example, two units of increase in average expected postoperative pain increased the odds of developing moderate

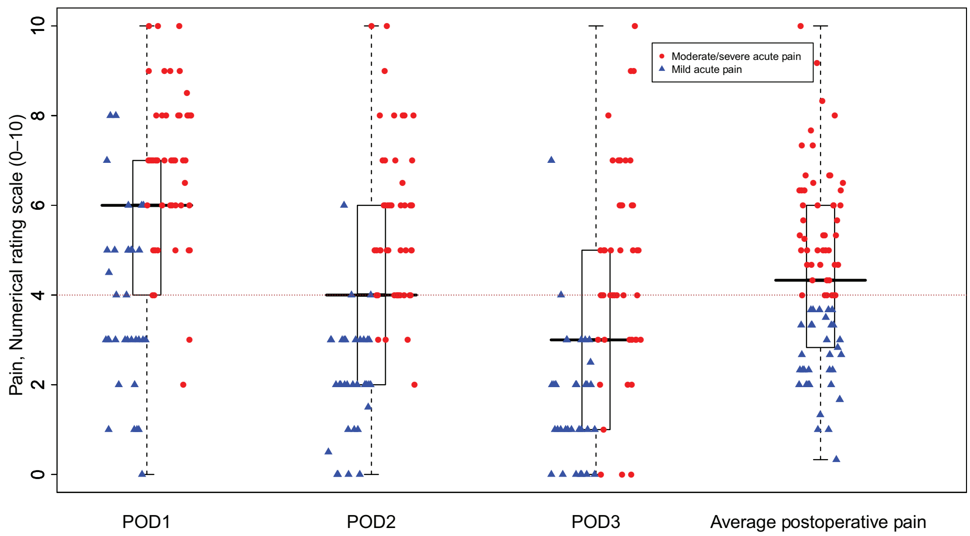

Figure 2. The average postoperative pain score was calculated as the mean of the pain scores from three postoperative days. Moderate to severe acute pain was defined when the average postoperative pain score (numerical rating scale [NRS], 0–10) was ≥4, represented with circles in the figure. Those patients with average postoperative pain score <4 (mild acute pain) are represented with triangles. Note that some patients may have daily pain scores <4 on postoperative days 1, 2, or 3, but with an average postoperative pain score ≥4. For example, see the circles on POD 3 below the NRS line of 4.0. POD = postoperative day.

to severe acute pain 1.8 times (NRS, 0–10; b = 0.27, 95% CI = 0.05 to 0.50). A bias-corrected 95% bootstrap CI for the indirect effect of pain to the suprathreshold cold stimulus was entirely above zero (ab = 0.063, 95% CI = 0.01 to 0.18). There was no evidence that pain to the suprathreshold cold stimulus influenced the moderate to severe acute pain independent of its effect on average expected postoperative pain (c' = 0.22, 95% CI = –0.03 to 0.48). Based on these results, it was concluded that the average expected postoperative pain is a partial mediator, and it accounted for 22% of the effect between pain to the suprathreshold cold stimulus and moderate to severe acute pain [34].

Acute Pain on the Continuous Scale

As an exploratory goal, the average postoperative pain score was also analyzed on a continuous scale (NRS, 0–10) rather than the binary outcome of mild (NRS < 4) vs moderate to severe (NRS ≥ 4) acute pain. Consistent with the binary outcome results, average expected postoperative pain is the only variable associated with average postoperative pain, and it mediated the effect of pain to the suprathreshold cold stimulus on average postoperative pain (data not shown).

Discussion

This is the first prospective study to consider a comprehensive list of preoperative, demographic, psychosocial, and surgical variables against acute pain after VATS. Factors univariately associated with the presence of moderate to severe acute pain after VATS were greater average expected postoperative pain, greater pain to a suprathreshold cold stimulus, and longer durations of surgery and hospital stay. When considered in the multiple logistic regression model, greater average severity of postoperative pain expected by patients when questioned preoperatively was the only variable associated with a higher likelihood of developing moderate to severe acute pain. Expected postsurgical pain mediated the effect of pain to the suprathreshold cold stimulus on moderate to severe acute pain. Contrary to our expectations, preoperative psychological factors were not associated with the development of moderate to severe acute pain.

Average Expected Postoperative Pain

When questioned preoperatively, the majority of subjects (73%) expected to develop moderate to severe acute pain. On average, patients expected 0.6 ± 2.3 NRS units higher than their postoperative NRS. The association of expected postoperative pain with acute pain is consistent with previous studies after breast cancer surgery [16,36] and cesarean section [13]. In a smaller population of adolescent surgical patients, anxiety and expected postoperative pain predicted acute pain [37]. Psychological factors and expected postoperative pain predicted acute pain in a large adult population as well [14]. The absence of preoperative pain for most VATS patients may contribute to the lack of association with any preoperative psychological measures in this study.

It is possible that some patients have a tendency to systematically rate the NRS higher across all levels of anticipated and perceived pain. To examine this association, the correlation coefficients of the quantitative sensory testing measures with the expected postoperative pain scores were assessed (Table 5). According to our data,

Table 1. Preoperative evaluation, approximately one week before video-assisted thoracic surgery

Variable	Moderate to Severe Acute Pain (Average Pain ≥ 4) (N = 48)	Mild Acute Pain (Average Pain < 4) (N = 34)	*P* Value
Age at surgery, mean ± SD, y	61.2 ± 10.9	60.7 ± 11.1	0.85
Male, No. (%)	30 (68)	14 (32)	0.056
Female, No. (%)	18 (47)	20 (53)	
ASA PS, No. (%)			0.56†
2	15 (52)	14 (48)	
3	29 (64)	16 (36)	
4	3 (50)	3 (50)	
History of tobacco use, No. (%)			0.19
Never smoked	10 (45)	12 (55)	
Former	26 (59)	18 (41)	
Current	12 (75)	4 (25)	
History of alcohol use, No. (%)			0.11
<2 drinks/d	42 (63)	25 (37)	
≥2 drinks/d	6 (40)	9 (60)	
Preoperative pain at rest (NRS, 0–10), median (Q_{25}, Q_{75}) [min, max]	0 (0, 0.5) [0, 4]	0 (0, 1) [0, 6]	0.82
Preoperative pain at rest > 0, No. (%)			0.88
Yes	12 (57)	9 (43)	
No	36 (59)	25 (41)	
Preoperative pain with cough (NRS, 0–10), median (Q_{25}, Q_{75}) [min, max]	0 (0, 0.5) [0, 6]	0 (0, 0) [0, 2]	0.13
Preoperative pain with cough > 0, No. (%)			0.14
Yes	12 (75)	4 (25)	
No	36 (55)	30 (45)	
Expected postoperative pain severity (NRS, 0–10), median (Q_{25}, Q_{75})			
Day 1	7.0 (5.0, 8.5)	5.0 (4.0, 8.0)	0.028
Day 2	6.0 (4.0, 7.0)	4.0 (3.0, 5.0)	0.006
Day 3	4.0 (2.3, 6.0)	2.0 (0.0, 4.0)	0.002
Average expected postoperative pain	5.8 (4.0, 7.3)	4.3 (2.3, 5.0)	0.005
QST cold degree °C, median (Q_{25}, Q_{75})	0 (0, 5.3)	0 (0, 1.13)	0.33
QST suprathreshold NRS (0–10), median (Q_{25}, Q_{75})	1.0 (0.0, 3.8)	0 (0, 1.0)	0.03
Preoperative chemotherapy within 6 wk of the surgery, No. (%)			0.41†
Yes	0 (0)	1 (100)	
No	48 (59)	33 (41)	
Preoperative radiation therapy within 6 wk of the surgery, No. (%)			1.0†
Yes	1 (100)	0 (0)	
No	47 (58)	34 (42)	
Prescribed opioid at the time of last preoperative clinic visit, No. (%)			0.18
Yes	8 (80)	2 (20)	
No	40 (56)	32 (44)	

Continuous variables are presented as either mean ± SD with a two-sample Student *t* test *P* value, or as median (first, third quartiles) with a Wilcoxon rank-sum test *P* value. Categorical variables are presented as frequency (%) with a chi-square test or †Fisher's exact test *P* value.

those patients with higher pain in response to the suprathreshold cold stimulus also reported higher expected pain scores. Similarly, those patients with higher expected pain scores reported higher acute pain.

Quantitative Sensory Testing

Based on a systematic review, preoperative QST may predict 4% to 54% of the variance in postoperative pain [38]. Two of the reviewed 14 studies were for thoracotomy patients. Consistent with our results, the first study reported that none of the preoperative QST measurements were associated with acute pain in the multiple logistic regression model [39], and the second study reported that none of the QST measures were associated postoperative pain at rest [15]. In our study, both expected pain and pain to the suprathreshold cold stimulus were univariately associated with moderate to severe acute pain. Interestingly, these two factors are interdependent; pain to the suprathreshold cold stimulus did not add any additional predictive value to the model. More studies are needed to determine the predictive ability of preoperative QST measurements for acute pain in the presence of expected pain in the model [40].

Table 2. Preoperative psychological assessments

Variable	Moderate to Severe Acute Pain (Average Pain ≥ 4) (N = 48)	Mild Acute Pain (Average Pain < 4) (N = 34)	*P* Value
Anxiety T, mean ± SD	52.4 ± 8.9	52.7 ± 8.2	0.91
Depression T, mean ± SD	49.1 ± 8.1	50.1 ± 7.1	0.59
Fatigue T, mean ± SD	49.6 ± 8.7	49.4 ± 9.7	0.93
Physical function T, mean ± SD	45.6 ± 8.8	48.7 ± 8.5	0.12
Sleep T, mean ± SD	49.5 ± 9.5	48.8 ± 8.9	0.75
PCS total score, median (Q_{25}, Q_{75})	21 (16, 26)	17 (14, 27)	0.22
PCS total score, No. (%)			0.83†
> 30	8 (57)	6 (43)	
≤ 30	38 (60)	25 (40)	
PCS rumination, median (Q_{25}, Q_{75})	8 (5, 11)	7 (4, 12)	0.40
PCS magnification, median (Q_{25}, Q_{75})	4 (3, 6)	4 (3, 5)	0.17
PCS helplessness, median (Q_{25}, Q_{75})	8 (6, 10)	7 (6, 10)	0.47
PTSD total score, median (Q_{25}, Q_{75})	22 (19, 28)	23 (20, 30)	0.50
AAQ total score, median (Q_{25}, Q_{75})	11 (8, 13)	8 (7, 13)	0.12

The results of the Patient-Reported Outcomes Measurement Information System questionnaires are presented as standardized T scores with a mean of 50 and an SD of 10. Therefore, a patient with a physical function T score of 40 is 1 SD below the US general population mean. Continuous variables are presented as either mean ± SD with a two-sample Student *t* test *P* value, or as median (first, third quartiles) with a Wilcoxon rank-sum test *P* value. Categorical variables are presented as frequency (%) with a chi-square test $^{\dagger}P$ value.

AAQ = Acceptance and Action Questionnaire (higher scores indicate greater emotional distress); PCS = Pain Catastrophizing Scale (lower score is better; for the normative data set, the 75th percentile was 30); PTSD = post-traumatic stress disorder (lower score is better).

Table 3. Intraoperative and early postoperative evaluation (days 0 to 3 after video-assisted thoracic surgery)

Variable	Moderate to Severe Acute Pain (Average Pain ≥ 4) (N = 48)	Mild Acute Pain (Average Pain < 4) (N = 34)	*P* Value
Procedure type,* No. (%)			
Lobectomy	23 (72)	9 (28)	0.05
Wedge resection	30 (60)	20 (40)	0.74
Biopsy/resection of lung nodule(s) or infiltrate	2 (40)	3 (60)	0.66
Other	1 (25)	3 (75)	0.30
No. of ports (%)			0.51†
0–2	7 (70)	3 (30)	
3+	41 (57)	31 (43)	
Duration of surgery, median (Q_{25}, Q_{75}), min	97 (51, 176)	61 (43, 120)	0.026
Duration of hospital stay, median (Q_{25}, Q_{75}), d	3 (2, 4)	2 (1, 3)	0.04
Average opioid consumption POD 0 to POD 3, median (Q_{25}, Q_{75}), morphine equivalent, mg	69 (50, 100)	62 (41, 72)	0.12
Epidural use (starting the day of surgery and up to 3 d after surgery), No. (%)			0.35†
Yes	8 (73)	3 (27)	
No	40 (56)	31 (44)	
Any chest tube on POD 1, No. (%)			0.057
Yes	43 (63)	25 (37)	
No	5 (36)	9 (64)	
Any chest tube on POD 2, No. (%)			0.26
Yes	20 (67)	10 (33)	
No	28 (54)	24 (46)	
Any chest tube on POD 3, No. (%)			0.50
Yes	13 (65)	7 (35)	
No	36 (56)	27 (44)	
Daily average pain intensity			
Day 1, median (Q_{25}, Q_{75})	7.0 (6.0, 8.0)	3.0 (3.0, 5.0)	
Day 2, median (Q_{25}, Q_{75})	5.0 (4.0, 7.0)	2.0 (1.5, 3.0)	
Day 3, median (Q_{25}, Q_{75})	5.0 (3.0, 6.0)	1.5 (1.0, 2.0)	
Average postop pain, median (Q_{25}, Q_{75})	5.3 (4.7, 6.4)	2.5 (2.0, 3.3)	
Average postop pain, mean ± SD	5.7 ± 1.4	2.5 ± 0.9	

Data are presented either as median (first and third quartiles) with a Wilcoxon rank-sum test *P* value or as frequency (%) with a chi-square test or †Fisher exact test *P* value.

*Some patients had more than one type of procedure. Therefore, the sum of procedure types is greater than 82.

Table 4. Simple and multiple regression models for the presence of moderate to severe acute pain during the first three days after video-assisted thoracoscopic surgery (N = 82)

	Simple Logistic Regression Model		Multiple Logistic Regression Model, Including All 6 Covariates	
Variable	Parameter Estimate (Standard Error)	*P* Value	Parameter Estimate	*P* Value
Average expected postoperative pain (NRS, 0–10)	0.31 (0.11)	0.007	0.31 (0.13)	0.02
QST suprathreshold NRS (0–10)	0.27 (0.12)	0.03	0.20 (0.14)	0.15
Duration of surgery, min*	0.82 (0.34)	0.02	0.37 (0.45)	0.41
Duration of hospital stay,* median (Q_{25}, Q_{75}), d	0.51 (0.33)	0.13†	0.24 (0.40)	0.54
Gender	0.87 (0.46)	0.06	1.16 (0.55)	0.04
Any chest tube on POD 1	1.13 (0.61)	0.07	0.32 (0.75)	0.68
The final model using the modified Poisson regression approach				
	Parameter Estimate (Standard Error)	*P* Value	RR (99% CI)	
Average expected postoperative pain (NRS, 0–10)	0.11 (0.04)	0.003	1.12 (1.02 to 1.23)	

The final model using the modified Poisson regression approach: Log(probability of moderate to severe average postoperative pain) = –1.13 + 0.11 average expected postoperative pain (C-statistic = 0.69).

CI = confidence interval; NRS = numerical rating scale; RR = relative risk.

*Durations of surgery and hospital stay variables were log-transformed.

†The *P* value for the Wilcoxon rank-sum test comparing duration of hospital stay is 0.04 (see Table 3). The *P* value for the log-transformed duration of hospital stay in the simple logistic regression model is 0.13.

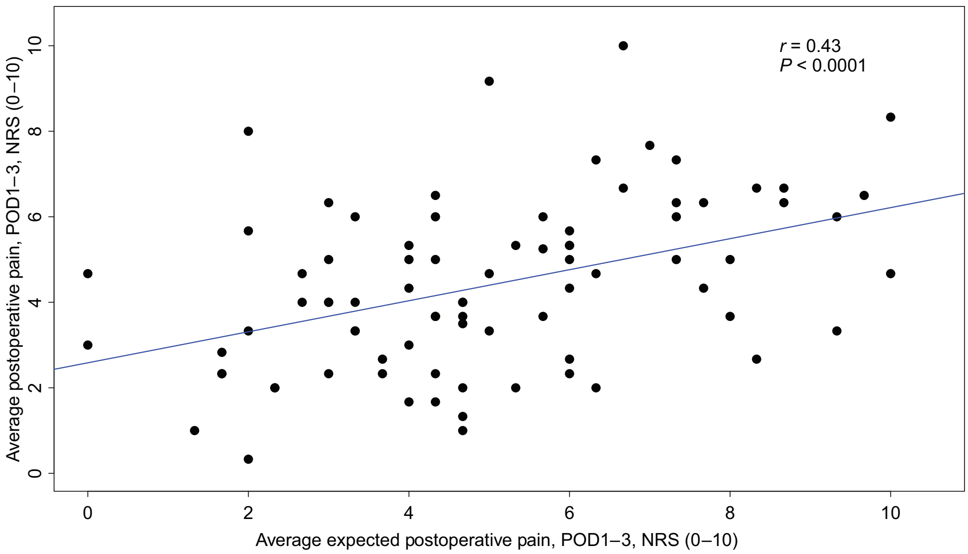

Figure 3. Average expected vs average observed postoperative pain severity scores during the first three days after VATS. NRS = numerical rating scale; POD = postoperative day.

Overall Pain

In other studies, pain was measured at a single time point [36,41] or the highest pain score was recorded [42] to classify a subject in a moderate to severe acute pain group. We measured the overall severity of pain for each of the first three PODs. With our classification, for example, patients with pain ratings of 7, 2, and 2—or 4, 4, and 3—during the first three PODs would be categorized in the mild pain group. Therefore, our method is conservative in terms of classifying patients as mild vs moderate to severe acute pain.

Preoperative Psychosocial Assessments

Preoperative or early postoperative psychosocial assessments are frequently used in acute pain studies [43]. We anticipated that some of the preoperative psychosocial measurements, especially the catastrophizing score, would be associated with the acute pain. However, similar to other preoperative psychological measures, catastrophizing was not associated with developing moderate to severe acute pain.

Preoperative catastrophizing [44,45] and anxiety [46] are associated with acute pain after anterior cruciate

Table 5. Correlation coefficients of preoperative expected postoperative pain with preoperative psychological assessments and quantitative sensory testing measures

Variable	Spearman Correlation Coefficient (*P* Value)
Anxiety T	0.19 (0.10)
Depression T	0.24 (0.03)
Fatigue T	0.17 (0.15)
Physical function T	–0.13 (0.25)
Sleep T	0.02 (0.88)
PCS total score	0.31 (0.01)
PCS rumination	0.20 (0.08)
PCS magnification	0.33 (0.003)
PCS helplessness	0.31 (0.007)
PTSD total score	0.04 (0.75)
AAQ total score	0.27 (0.02)
QST suprathreshold NRS (0–10)	0.23 (0.04)
QST cold degree °C	–0.07 (0.52)

AAQ = Acceptance and Action Questionnaire (higher scores indicate greater emotional distress); PCS = Pain Catastrophizing Scale (lower score is better; for the normative data set, the 75th percentile was 30); PTSD = posttraumatic stress disorder (lower score is better).

ligament repair and total knee arthroplasty. However, most patients with such surgeries have preoperative pain. Perhaps the PCS is a poor tool for predicting postoperative pain intensity when pain is not present preoperatively. The absence of preoperative pain for most VATS patients may contribute to the lack of association with any preoperative psychological measures in this study. In addition, we do not know how to categorize expected pain severity into the biopsychosocial/cultural model. Perhaps expected pain simply reflects the extent to which patients anticipate future pain, but catastrophizing is more about the cognitive and emotional impact of the current pain. Psychosocial measures may be assessed both preoperatively and during the acute pain phase after the procedure for future studies examining acute pain after VATS. Some preoperative psychosocial variables such as depression, acceptance and action, and catastrophizing were weakly correlated with expected pain ($P < 0.05$) (Table 5). However, none of these variables were associated with moderate to severe acute pain (Table 2). Therefore, the data suggest that preoperative expectations had greater predictive value than other variables that are considered in this study, including depression and catastrophizing. It is possible that the impact of these psychosocial factors would be more apparent if the sample size of the study was larger.

Study Limitations

First, the original prospective observational study was designed to examine chronic pain after thoracic surgery. Therefore, post hoc analyses were performed in the current study. Second, because of the observational nature of the study, the anesthetics utilized were not standardized [47,48] but followed usual care. For example, the postoperative use of acetaminophen and nonsteroidal anti-inflammatory drugs was not standardized. Epidural analgesia did not move all patients to the mild pain group; eight of the 11 patients were in the moderate to severe group. We also examined ketamine use. Ketamine was only given on induction to some of the patients. We compared the ketamine dose between the patients with moderate to severe acute pain (0.43 ± 0.17) vs mild acute pain (0.45 ± 0.16), and there was no difference ($P = 0.7$). There was also no difference in the proportion of patients receiving any dose of ketamine in the mild (15/34, 44%) vs moderate to severe pain groups (17/48, 35%, $P = 0.57$). Third, the sample size of the study was not based on the power calculations for the acute pain outcome. The rule of thumb for sample size calculations for the multiple logistic regression model is 10 patients per covariate in the smaller sample size group [49]. Our model has 34 patients in the mild acute pain group; therefore, it would accommodate three variables. We tested the associations of six variables. We used the type I error rate of 0.01 to guard against false discovery.

Conclusions

Average intensity of expected postoperative pain reported during the preoperative period was the only variable associated with the development of moderate to severe acute pain after VATS. It also mediated the effect of pain to a suprathreshold cold stimulus on acute pain. In our previous study, severity of acute pain was the only predictor of chronic pain after thoracic surgery. Expected pain is an important variable that predicts acute pain in a patient population at risk for chronic pain after surgery. More studies are needed to assess the utility of expected pain to predict acute pain in specific surgeries.

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