Original Article

The incidence and risk factors of acute pain after preoperative needle localization of pulmonary nodules: a cross-sectional study

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Background: The incidence, severity and associated risk factors of acute pain after preoperative needle localization of pulmonary nodules are poorly characterized. We therefore conducted a cross-sectional study to quantify the acute pain induced by preoperative needle localization of small pulmonary nodules before video-assisted thoracoscopic surgery (VATS).

Methods: We conducted this study at Shanghai Chest Hospital from September 2021 through December 2021. Eligible patients were between 18 and 75 years old and had small pulmonary nodules requiring preoperative CT-guided needle localization. The intensity of acute pain was assessed using the visual analogue scale (VAS) after preoperative needle localization. A VAS score ≥4 cm indicated moderate to severe pain. Patient demographics and CT-guided localization factors were collected to identify significant predictors associated with moderate to severe pain.

Results: A total of 300 patients were included in the final analysis, with a mean (SD) age of 51 (SD =12) years old; 63% were female. Moderate to severe pain occurred in 50.8% of patients during deep breathing and 45.7% of patients during movement. Multivariate logistic regression analysis showed that multiple localization needles [multiple needle localizations *vs.* single needle localization, odds ratio (OR): 2.363, 95% confidence interval (CI): 1.157–4.825, P=0.018] and the specific location of needle puncture on the chest wall were significant predictors of moderate to severe pain after CT-guided needle localization (lateral chest wall *vs.* anterior chest wall OR: 2.235, 95% CI: 1.106–4.518, P=0.025; posterior chest wall *vs.* anterior chest wall OR: 1.198, 95% CI: 0.611–2.349, P=0.599).

Conclusions: In adult patients receiving hookwire CT-guided localization, moderate to severe pain was common. Avoiding the localization route through lateral chest wall may be helpful and pharmacological medications or regional blockade is necessitated in high-risk population.

Keywords: Small pulmonary nodules; lung cancer; CT-guided localization; pain; complications

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Introduction

As increasing numbers of people undergo lung cancer screening by low-dose computed tomography (CT), millions of small pulmonary nodules (<1 cm in size) or ground-glass opacities (GGOs) are detected early (1-3). Among those small pulmonary nodules or GGOs, a substantial percentage of nodules may require video-assisted thoracic surgery (VATS) to intervene (1). However, these small pulmonary nodules are difficult to be identified under VATS and thoracic surgeons often need to perform preoperative CT-guided localization to accurately localize the nodules intraoperatively (4-6).

Until recently, none of the available preoperative CT-guided localization methods are optimal and may predispose patients to potential harm (7,8). Among the preoperative CT-guided localization methods, hookwire localization remains the mainstay (9-11), but it may also lead to complications or significant risks (e.g., pneumothorax, pulmonary hemorrhage, substantial pain, and wire dislodgement) (12). The majority of previous studies mainly focused on the efficacy and safety of hookwire needle localization (7,8), but the related pain is not fully examined. A retrospective study involving 57 patients reported that the incidence of pain after hookwire localization was 7%, but they did not clearly state the method used to assess pain nor at which state (13). Other studies assessed pain as the exploratory component of complications after hookwire localization (14,15), but the severity and related risk factors are still limited. Exploring potential predictors may be helpful to prevent acute pain in high-risk population.

Based on our institutional experience, patients often experience moderate to severe pain after CT-guided localization before VATS. If not controlled well, acute pain after needle localization may cause severe discomfort or anxiety in patients. Herein, we conducted a cross-sectional study in a tertiary center, aiming to accurately determine the incidence and risk factors of acute pain after hookwire CT-guided localization. Specifically, we investigated the incidence of pain at rest, during deep breathing and movement after CT-guided localization and explored potential risk factors related to substantial acute pain. We present the following article in accordance with the STROBE reporting checklist (available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-22-557/rc).

Methods

Ethics and registration

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of Shanghai Chest Hospital (IRB #KS (P) 2142) and informed consent was taken from all the patients. This trial was registered at the Chinese Clinical Trial Registry prior to subject enrolment (No. ChiCTR2100051447; principal investigator, Yuwei Qiu; date of registration, September 23, 2021).

Patients and study design

This cross-sectional study was conducted at Shanghai Chest Hospital. Eligible patients were between 18 and 75 years old, had an American Society of Anesthesiologists (ASA) physical status of I–III, were scheduled for elective video-assisted thoracoscopic surgery, and had small lung nodules requiring preoperative CT-guided localization.

Patients were excluded if they had clinically significant cardiovascular diseases, were unable to perform the visual analogue scale (VAS) (16), or had undergone previous thoracic surgeries, received chronic pain medication, were diagnosed with herpes zoster accompanied by debilitating pain, or other factors that precluded an accurate pain assessment.

Preoperatively, the patients were admitted to radiology procedure suite for localization. Local anesthesia using 2% lidocaine was administered for all patients by the radiologists performing localization. First, the position of the small pulmonary nodules was determined by high-resolution CT scanning (SIEMENS, SOMATOM Force, Bayern, Germany). Next, a localization needle (20# gauge size and length of 9 mm, GHIATAS Beaded Breast Localization Wire, Bard Peripheral Vascular Inc., Arizona, United States) or a disposable pulmonary nodule locating needle (model: SS510-10 Senscure, Ningbo, China) was used for localization (*Figure 1*). When the hook was released, an anchor needle would firmly grasp the adjacent lung tissue. CT reexamination was then used to confirm the positional relationship between the locating needle and the pulmonary nodules. VATS surgery was performed within 1–2 hours.

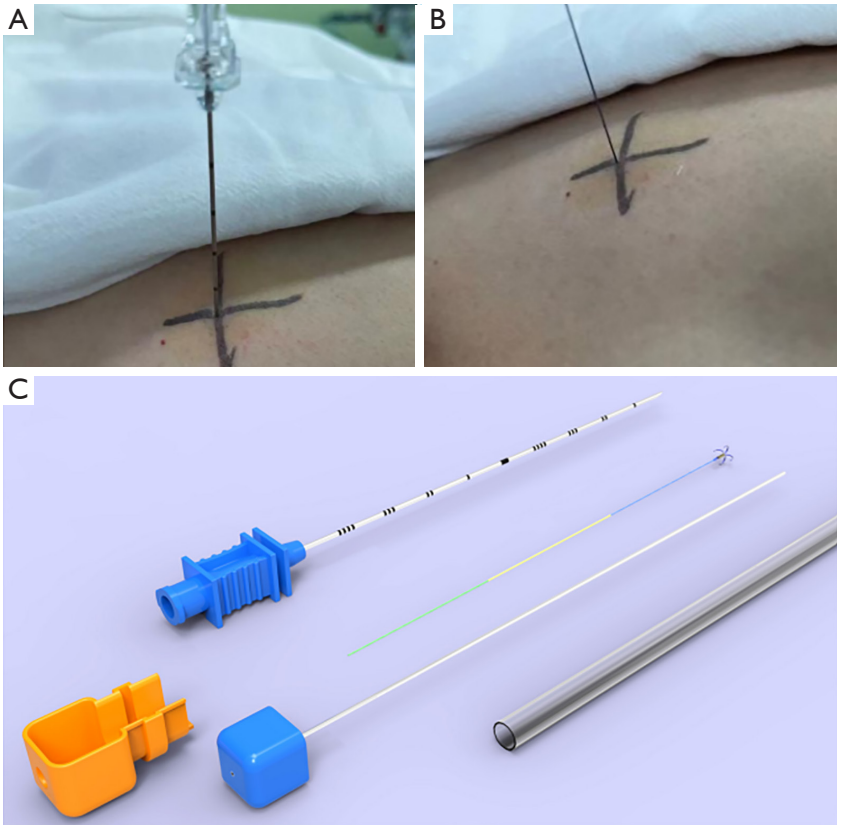

Figure 1 CT-guided needle localization. (A,B) GHIATAS Beaded Breast Localization Wire. (C) Senscure localization needle. CT, computed tomography.

Outcome assessment

Primary outcome

The primary outcome of this study was the incidence of moderate to severe pain during deep breathing after CT-guided needle localization.

10–15 minutes after needle localization, an investigating researcher assessed pain intensity using a 10 cm VAS (0 cm = no pain and 10 cm = worst imaginable pain) in the preanesthesia room (16). We assessed pain at rest, during deep breathing and physical movement (defined as moving the ipsilateral arm). Furthermore, we graded the pain severity of the VAS using the specific adjectives: 0 cm = no pain, 1–3 cm = mild pain, 4–6 cm = moderate pain, and 7–10 cm = severe pain) (16). A VAS score ≥4 cm was considered to indicate moderate to severe pain (16).

Exposure variables

The predefined exposure variables were based on the existing literature or clinical experience. The potential predictors of acute pain included patient demographics [age, gender, and body mass index (BMI), education levels (middle school, high school, or above)], preoperative psychological stress and CT-guided localization factors. The Chinese version of the State-Trait Anxiety Inventory (STAI) was used to reflect patients' psychological stress before CT-guided needle localization (17). STAI is a reliable instrument used to test both the levels of state and trait anxiety, in which the state anxiety reflects an immediate state of patients' anxiety at a particular moment (18,19). CT-guided localization factors included the numbers of localization needles, surgical site (left thorax, right thorax, and bilateral thorax), type of localization needles (GHIATAS Beaded Breast Localization Wire or Senscure localization needle), distance between the skin and final needle position around the lung lesion, distance between the parietal pleura and final needle position around the lung lesion, and the specific location of the needle puncture on the chest wall. Here, we classified the location of needle punctures on the chest wall into the following categories: anterior chest wall

(defined from the parasternal line to the anterior axillary line), lateral chest wall (defined from the anterior axillary line to the posterior axillary line), and posterior chest wall (defined from the posterior axillary line to the spine).

Other outcomes

Patients' vital signs including non-invasive systolic blood pressure, diastolic blood pressure, and pulse rate after needle localization were monitored and collected.

Statistical analysis

Statistical analyses were performed using SPSS software, Version 25 of the SPSS System (IBM, USA). Descriptive data were presented as mean ± standard deviations (SD), median (interquartile ranges), or percentage. One-way ANOVA was applied for between-group testing of continuous variables. The Chi-square or Fisher's Exact tests were used for categorical variables.

Multivariable logistic regression models were developed to examine the predictors of moderate to severe pain during deep breathing after hookwire CT-guided needle localization. Acute pain intensity during deep breathing was differentiated as "moderate to severe pain" *vs.* "mild or no pain" according to the VAS. Factors with P<0.1 in the univariate analysis were evaluated as potential covariates in stepwise multivariable logistic regression analyses with forward selection. Multivariate stepwise logistic regression was performed on all variables retained from the univariate analysis. A *post-hoc* analysis included a comparison between the identified risk factors in terms of acute pain intensity. A two-sided significance level of 5% (P<0.05) and confidence intervals (CIs) of 95% were used.

Our sample size was determined as follows. The primary outcome of this study was the incidence and risk factors of moderate to severe pain during deep breathing after CT-guided needle localization. However, research was limited regarding the true incidence of pain, thus we conducted a pilot study and found that the incidence of moderate to severe pain at deep breath was 48% (24/50). We planned to include 300 patients and estimated to have about 150 events, which should be more than sufficient for testing 9 predictors under the rule of thumb of 10 events per predictor (20).

Results

A total of 335 patients were screened for inclusion between September 24, 2021 and December 31, 2021. After excluding 35 patients (18 patients had rescheduled their surgery, 9 patients refused to participate, 2 patients had preoperative fever, and 6 patients had canceled preoperative CT-guided localization), 300 patients were included in the final analysis (*Figure 2*). All patients were followed up according to the study protocol.

The mean age of the patients was 51 (SD =12) years, and 63% were female. GHIATAS beaded breast localization wire was used in 88.7% of the patients and Senscure localization needle was used in 11.3%. Single needle localization was achieved in 76.3% of the patients, with the remaining 23.7% having two or more needle localizations for multiple pulmonary nodules. Needle localization on the specific chest wall occurred in 268 (89%) patients and 32 (11%) patients received needle localization on mixed locations of the chest wall. The mean procedure time for CT-guided hookwire localization was 8 min (range, 5–10 min). The patients' demographics and localization-related variables are shown in *Table 1* and *Table 2*.

Prevalence of acute moderate to severe pain after CT-guided needle localization

After CT-guided pulmonary nodule localization, 17.8% of the patients had a VAS between 4 and 6 cm and 2.3% had a VAS between 7 and 10 cm at rest. However, during deep breathing, acute pain was more prevalent, with 41.1% of patients experiencing a VAS between 4 and 6 cm and 9.7% with a VAS between 7 and 10 cm. In total, moderate to severe pain during deep breathing or movement occurred in 50.8% and 45.7% of patients respectively, as shown in *Table 2*.

Predictors of moderate to severe pain during deep breathing

Univariate analysis showed that age (P=0.068), number of localization needles (P=0.029), and the specific location of the puncture on the chest wall (P=0.024) were potential risk factors related to moderate to severe pain during deep breathing (*Table 3*).

Multivariate logistic regression analysis showed that multiple needle locations (compared to single needle location: OR: 2.363, 95% CI: 1.157–4.825, P=0.018) and the specific location of the needle punctures on the chest wall (lateral chest wall versus anterior chest wall OR: 2.235, 95% CI: 1.106–4.518, P=0.025; posterior chest wall versus

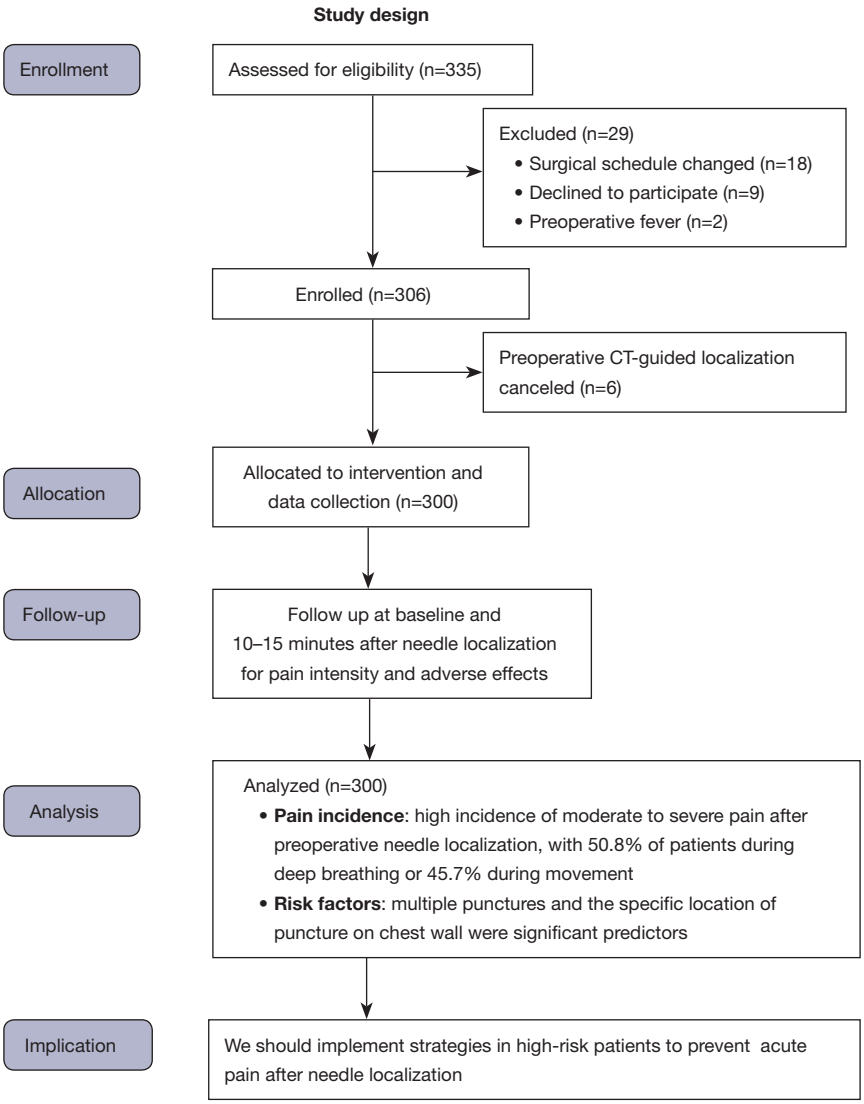

Figure 2 Graphic abstract.

anterior chest wall OR: 1.198, 95% CI: 0.611–2.349, P=0.599) were identified as significant predictors of moderate to severe pain after CT-guided needle localization (*Table 3*). Other factors included in this study (i.e., age, sex, BMI, educational level, preoperative level of anxiety, type of needles, direction of needle puncture, and distance from the skin to the tips of the needles) were not related to moderate to severe pain (P>0.05, *Table 4*).

Post-hoc analysis

Non-parametric tests were used to compare the effect of the specific location of needle puncture on acute pain intensity. The results showed that there were significant differences between the three locations of needle puncture on the chest wall (P=0.036). The median VAS (interquartile ranges) was 3 [2–4] cm, 4 [3–5] cm, and 3 [2–5] cm in the anterior chest wall, lateral chest wall, and posterior chest wall, respectively (*Table 2*).

Association between acute pain intensity during deep breathing and patients' other outcomes

We did not find that there were any differences in systolic blood pressure, diastolic blood pressure, and pulse rate between patients regardless of whether or not they

Table 1 Demographics and clinical characteristics of patients with pulmonary nodules for localization

Variables	Mean ± SD or n (%) (N=300)
Age (years)	51±12
Sex	
Female	190 (63.3)
Male	110 (36.7)
ASA physical status	
I	186 (62.0)
II	96 (32.0)
III	18 (6.0)
Body mass index (kg/m^2)	23.0±3.0
Educational level	
Middle school	100 (33.3)
High school or above	200 (66.7)
Smoking status	
Current	16 (5.3)
Former	45 (15.0)
Never	239 (79.7)
Alcohol use	
Current	31 (10.3)
Former	17 (5.7)
Never	252 (84.0)
Comorbidities	
Hypertension	67 (22.3)
Diabetic mellitus	24 (8.0)
Coronary heart disease	5 (2.0)
Arrhythmia	8 (2.7)

ASA, American Society of Anesthesiologists.

Table 2 Localization characteristics in patients with pulmonary nodules for localization

Variables	N=300
Localization characteristics	
Numbers of location needles, n (%)	
1	229 (76.3)
2	62 (20.7)
3	9 (3.0)
Types of localization device, n (%)	
GHIATAS Beaded Breast Localization Wire	266 (88.7)
Senscure localization needle	34 (11.3)
Direction of thorax, n (%)	
Left thorax	114 (38.0)
Right thorax	181 (60.3)
Bilateral thorax	5 (1.7)
Specific location of puncture on chest wall, n (%)	
Anterior chest wall	52 (17.3)
Lateral chest wall	92 (30.7)
Posterior chest wall	124 (41.3)
Mixed	32 (10.7)
Distance from skin to needle tip, mm	63±16
Distance from parietal pleura to needle tip, mm	23±13
Mean procedure time, min	8 [5, 10]
Pain characteristics	
Median VAS of pain at rest, cm	2 [2, 3]
Proportions of pain at rest, n (%)	
VAS 0–3	240 (79.9)
VAS 4–6	53 (17.8)
VAS 7–10	7 (2.3)
Median VAS of pain during deep breathing, cm	4 [2, 5]
Proportions of pain during deep breathing, n (%)	
VAS 0–3	148 (49.2)
VAS 4–6	123 (41.1)
VAS 7–10	29 (9.7)
Median VAS of pain during movement, cm	3 [2, 5]
Proportions of pain during movement, n (%)	
VAS 0–3	163 (54.3)
VAS 4–6	106 (35.3)
VAS 7–10	31 (10.3)
Median VAS among different specific chest wall locations	
Anterior chest wall	3 [2, 4]
Lateral chest wall	4 [3, 5]
Posterior chest wall	3 [2, 5]
Rescue medication, n (%)	16 (5.3)
Median of pre-procedural state anxiety	47 [45, 49]

Data are presented as mean (standard deviation) or median [inter-quartile range], or n (%). VAS, visual analogue scale.

experienced moderate to severe pain. Furthermore, 5.3% (16/300) of patients were treated with cyclooxygenase-2 (COX-2) inhibitors without perceptible relief.

Discussion

This cross-sectional study was the first to thoroughly investigate acute pain following preoperative localization of pulmonary nodules. About a half of the patients included in this study experienced moderate to severe pain after preoperative needle localization, including 50.8% of patients during deep breathing and 45.7% during movement. We found that multiple punctures and the specific locations of punctures on the chest wall were significantly associated with moderate to severe pain after preoperative needle localization, irrespective of age, gender, BMI, levels of preoperative anxiety, type of needles, direction of needle punctures, or penetration depth.

Initially developed for the localization of breast nodules, hookwire has been widely applied for the localization of pulmonary nodules in China since 2009 (21), and involves passing a puncture needle directly through the lung tissue to anchor the lesion. Previous research has mainly focused on the safety and efficacy of hookwire localization during VATS resection (1,12,19,21). Hookwire localization has a high localization accuracy, short operation time, and few postoperative complications, and is therefore well suited to detect small pulmonary nodules in thoracic centers (22,23). However, this method still has some limitations. Patients may feel substantial pain or discomfort due to the rigid wire traversing the chest wall and remaining in place until surgical resection (24,25), and some patients appear unable to lie still due to severe pain.

There are no studies that thoroughly investigate acute pain after needle localization prior to VATS. Yoshida *et al.* reported that the incidence of pain after hookwire localization was 7%, but they did not clearly state which method was used (13). Hu *et al.* compared the efficacy and safety of localization of small pulmonary nodules with microcoil and hookwire (26). Their data found that 24.2% (8/33) of patients in the hookwire group experienced moderate to severe pain at rest (26). We found that 20.1% of patients experienced moderate to severe pain at rest, which was consistent with Hu *et al.*'s findings. In our study, pain was assessed at different statuses including at rest, during deep breathing, or movement. Patients reported the pain as localized, sharp, and constant at rest, which was greatly aggravated by deep breathing or movements such as turning in bed, sitting or changing directions in our study. Possible sources of nociceptive input of preoperative needle localization remained unclear and might be multifactorial. We assumed that this mechanism is related to needle puncture of the skin or muscles, intercostal nerve injury, or irritation and inflammation of the lung parenchyma or pleura. As mentioned above, hookwire localization anchored the small pulmonary nodules by inducing the rigid wire from the skin to the lung parenchyma, and then keeping the rigid wire in place until surgical resection. Although the needle puncture was performed under local infiltration with 2% lidocaine, the rigid wire may also damage muscles, cause lesion to the intercostal nerve, or provoke visceral pain of the lung parenchyma, ultimately leading to moderate to severe pain.

We found that two specific factors were associated with the increased incidence of moderate to severe pain during deep breathing: additional numbers of penetration needles and the penetration location on the chest wall. Tian *et al.* reported that multiple punctures increased the incidence of pneumothorax and intrapulmonary hemorrhage compared with single puncture during CT-guided microcoil localization of pulmonary nodules (27), but they did not analyze differences in pain. Our data indicates that compared to a single puncture, multiple punctures with more than one needle may increase to increase the risk of moderate to severe pain by two-fold. Multiple punctures with more than one needle may increase the risk of damage to the muscles, intercostal nerves, bony structure, and pulmonary parenchyma or pleura. We speculate that this was similar to the fact that a single chest tube was associated with less pain without increasing the risk of recurrent effusion compared to the routine two chest drainage tubes (28). Interestingly, the specific location of needle punctures on the chest wall contributed to a substantial proportion of acute pain. Previous reviews have reported that the intercostal nerves aroused from the ventral rami of the thoracic spinal nerves and were mixed with both sensory and motor fibers. The collateral branch of the intercostal nerves provides sensory innervations to the pleura, peritoneum, partial anterior, and lateral chest walls (29). Damage or irritation to the intercostal nerves may affect thoracic pain. In our results, the lateral chest seemed to be the most vulnerable region of pain, and was statistically significant compared to the anterior-lateral area. This might result from increased likelihood of intercostal nerve injury. Similarly, some evidence has demonstrated that the incidence of long-term pain after sternotomy

Table 3 Descriptive differences in predictor variables (between those that developed moderate to severe pain and those that did not) during deep breathing after preoperative CT-guided needle localization

Variable	Moderate to severe pain during deep breathing after needle localization		
	Absent (n=148)	Present (n=152)	P value
Age, years	52±12	49±12	0.068[$]
Female, n (%)	88 (59.5)	102 (67.1)	0.169
Educational level, n (%)			0.235
High school or above	104 (70.3)	97 (63.8)	
Middle school	44 (29.7)	55 (36.2)	
Body mass index (kg/m^2)	23.12±3.01	22.82±2.82	0.383
Pre-procedural State Anxiety	47±3	47±3	0.363
Direction of thorax[!]			0.370
Left thorax	60 (41.4)	55 (36.7)	
Right thorax	85 (58.6)	95 (63.3)	
Numbers of needles			0.029*
Single needle location	121 (81.8)	108 (71.1)	
Multiple needle location	27 (18.2)	44 (28.9)	
Specific location on chest wall[&]			0.024*
Anterior chest	35 (24.0)	28 (19.6)	
Lateral chest	42 (28.8)	60 (41.9)	
Posterior chest	69 (47.3)	55 (38.5)	
Types of location device, n (%)			0.265
GHIATAS Beaded Breast Localization Wire	129 (87.2)	137 (90.1)	
Senscure location needle	19 (12.8)	15 (9.9)	
Systolic blood pressure after localization	135±19	134±24	0.483
Diastolic blood pressure after localization	82±11	81±13	0.335
Pulse rate after localization	75±8	75±9	0.627

Data are presented as mean ± standard deviation, median (inter-quartile range), or n (%). Variables when [$]P<0.1 were included in final multivariate model. *, significant difference between groups (P<0.05). [!], patients localized at bilateral thorax are not included in the analysis here. The actual total number of patients are 145 in Absent column and 150 in Present column. [&], patients with mixed locations on the chest wall are not included in the analysis. The actual total number of patients are 146 in Absent column and 143 in Present column.

Table 4 Final multivariate model of predictors of moderate to severe pain during deep breathing after preoperative CT-guided needle localization

Variables	Z	P value	OR	95% CI
Age per year increase	1.201	0.273	0.989	0.969–1.009
Multiple location needles *vs.* single location needle	5.570	0.018*	2.363	1.157–4.825
Specific location on the chest wall				
Lateral *vs.* anterior	5.020	0.025*	2.235	1.106–4.518
Posterior *vs.* anterior	0.277	0.599	1.198	0.611–2.349

*, significant difference (P<0.05). OR, odds ratio; CI, confidence interval.

or anterior thoracotomy was less than that after lateral thoracotomy (30). In terms of specific neurophysiological studies on the role of nerve damage during persistent pain in thoracotomy, Benedetti *et al.* found evidence of nerve damage in both acute and chronic pain following posterolateral thoracotomy (31). Anterior thoracotomy was less likely to cause nerve dysfunction compared with the posterolateral approach (32).

Some studies have explored new devices that could impact soft tissue injury and therefore mitigate the pain response. A semi-rigid hookwire was reported to have an improved ease of use compared to a double-thorn hookwire or microcoil, representing a promising therapeutic direction (32). A multicenter, prospective study of a novel technique for pulmonary nodule localization found that Senscure needles had a high success rate, feasibility, and good tolerance in all patients, without significant pain (14). Contrary to Fan *et al.*'s findings (14), we did not observe that Senscure needles were associated with less pain. A possible explanation for this discrepancy may be that only 11.3% of patients underwent localization using Senscure location needles, as compared to 88.7% of patients who received GHIATAS. The higher cost of Senscure's needle may restrict its application in clinical practice.

Our cross-sectional study has some strengths to explore risk factors of acute pain after CT-guided localization of pulmonary nodules. However, limitations still exist. Firstly, this was a single-center observational study and undoubtedly had inherent limitations. Secondly, we did not include the effect of procedure proficiency on acute pain. In our center, CT-guided localization was primarily conducted by the radiologist team in which each radiologist performed 1,000 consecutive cases every year. This substantial procedural experience allowed radiologists to achieve very favorable localization outcomes. Thirdly, we assessed acute pain at 10–15 minutes after needle localization when the initial pain was stable. However, the pain intensity may change as time passed. Finally, whether acute pain was associated with complications due to CT-guided localization (pneumothorax or hemorrhage) was uncovered in our study and should be addressed in the future.

In summary, moderate to severe acute pain during deep breathing or movement after preoperative localization of pulmonary nodules is very common. The number of localization needles and the specific location of punctures on the chest wall were identified to be significant predictors of moderate to severe pain. As with all observational analyses, causality cannot be assumed, and more trials are needed to further verify our results. Awareness of the potential risk factors for moderate to severe acute pain might reduce the incidence after CT-guided localization and allow for the implementation of preventative strategies accordingly.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-22-557/rc

Data Sharing Statement: Available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-22-557/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-22-557/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 Institutional Review Board of Shanghai Chest Hospital (IRB #KS (P) 2142) and informed consent was taken from all the patients.

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