Original Article

# Computed tomography-guided hookwire localization and medical glue combined with methylene blue localization for pulmonary nodules before video-assisted thoracoscopic surgery: a single-center, retrospective study

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**Background:** The aim of this study was to investigate the safety and efficacy of computed tomography (CT)-guided hookwire localization and new CT-guided medical glue combined with methylene blue (MGMB) localization before video-assisted thoracoscopic surgery (VATS) for solitary pulmonary nodules (SPNs) and to analyze the risk factors for complications after localization.

**Methods:** A total of 620 patients, comprising 727 SPNs, admitted to the Department of Thoracic Surgery of the First Hospital of the University of Science and Technology of China between December 2019 and July 2022 were retrospectively studied and case-control analyzed. According to the localization method, 620 patients were divided into the hookwire group (n=310) and MGMB group (n=310). The localization time, localization-to-surgery interval, operative time, length of hospitalization, and complication rate were compared between the 2 groups. Logistic regression was used to analyze the risk factors for the occurrence of complications in each group of localization methods.

**Results:** Compared to the hookwire group, the MGMB group had a shorter localization time (8.59±3.69 *vs.* 7.35±2.99 min; P<0.001), shorter hospital stay (5.60±2.13 *vs.* 6.73±2.86 days; P<0.001), and shorter operative time (103.48±54.11 *vs.* 98.59±49.92 min; P=0.33). The preoperative localization success rate was 99.4% (355/357) and 100% (370/370) in the hookwire group and MGMB group, respectively. No death or serious complications occurred during the localization process, but the overall complication rate was lower in the MGMB group (69/310, 22.3%) than in the hookwire group (105/310, 33.9%) (P<0.001). Logistic regression analysis showed that age, number of nodules, and localization time were risk factors for total complications, while localization technique was a protective factor for total complications [odds ratio =0.590; 95% confidence interval (CI): 0.405–0.860; P<0.05].

**Conclusions:** Both techniques could effectively locate SPNs before VATS; however, MGMB localization was found to be associated with a lower complication rate, shorter localization time, better safety, and higher potential clinical value and is thus worthy of clinical promotion.

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## Introduction

After female breast cancer (11.7%), lung cancer is the second most commonly diagnosed cancer worldwide, with an estimated 2.2 million new cases (11.4%) occurring each year. It is also the leading cause of cancer death globally (1), and in China, it ranks first in the cancer death for both genders (male: 29.26%; female: 22.96%) (2,3).

A solitary pulmonary nodule (SPN) is a single lung nodule that is usually <3 cm. An SPN is a benign lesion but may also represent an early stage of lung cancer. With the popularity of regular physical examination and the widespread use of low-dose chest computed tomography (LDCT), the detection rate of SPNs has significantly increased (4,5). About 60–70% of SPNs or ground glass nodules (GGNs) are still in the early stages of the disease; however, if their solid component is >50% and they have high density, this often indicates a high possibility of malignancy. Most of the persistent GGNs are malignant or tend to progress to malignancy. An increased diameter of the nodule on follow-up or the solid component usually suggests malignant transformation and requires a puncture biopsy or surgical excision (6-8).

In recent years, video-assisted thoracoscopic surgery (VATS) has become the primary modality for treating SPNs by virtue of its association with minimal trauma and rapid postoperative recovery (9,10). However, in some small SPNs that are located far from the pleura, the surface lung tissue often has no specific mark, leading to difficulties in intraoperative localization and the necessity of converting to open surgery (11-13). Accurate localization of SPNs can guide the identification and resection of SPN during VATS and reduce the conversion rate to open thoracotomy. Therefore, adopting safe and effective individualized localization techniques is essential for ensuring surgical results.

Many prominent surgeons and interventional radiologists have developed various localization strategies to address this issue. Commonly used methods include the use of computed tomography (CT)-guided metal implants (microcoil and hookwire), the injection of liquid fluorescent dye [indocyanine green (ICG) and methylene blue], and the injection of medical glue (14-16). Hookwire and microcoil are widely used as metal tags for localization due to their high success rate. However, it has been suggested that their invasive nature may cause complications, including patient discomfort, pneumothorax, and pulmonary hemorrhage. After the localization procedure, coils are placed on the lung-to-skin surface until surgery, and breathing-related movements may cause the tags to shift (5,17). In contrast, visual dyes such as ICG and methylene blue are also commonly used for the localization of lung nodules owing to their safety and excellent penetration. However, as a liquid fluorescent dye, the dye solution quickly and rapidly diffuses into the surrounding lung parenchyma and visceral pleura, which may reduce the localization accuracy. Moreover, pleural irritation caused by the dye may cause discomfort to the patient. Therefore, some researchers suggest VATS treatment within 3 hours after methylene blue injection (4,18). In addition, ICG has limited tissue penetration at a depth of 24 mm and is not suitable for deep localization (5,19,20). The operability, safety, and efficacy of these localization methods used individually or in combination remain topics of contention.

The aim of this study was thus to investigate the safety and efficacy of CT-guided hookwire localization and new CT-guided medical glue combined with methylene blue (MGMB) localization in preoperative localization of VATS in SPNs and to analyze the risk factors for complications after localization. We present this article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-22-1240/rc).

## Methods

### *Patients*

A total of 620 patients with SPNs admitted to the Department of Thoracic Surgery of the First Affiliated Hospital of University of Science and Technology of China from December 2019 to July 2022 were retrospectively analyzed. Among these patients, 247 were males and 373

 

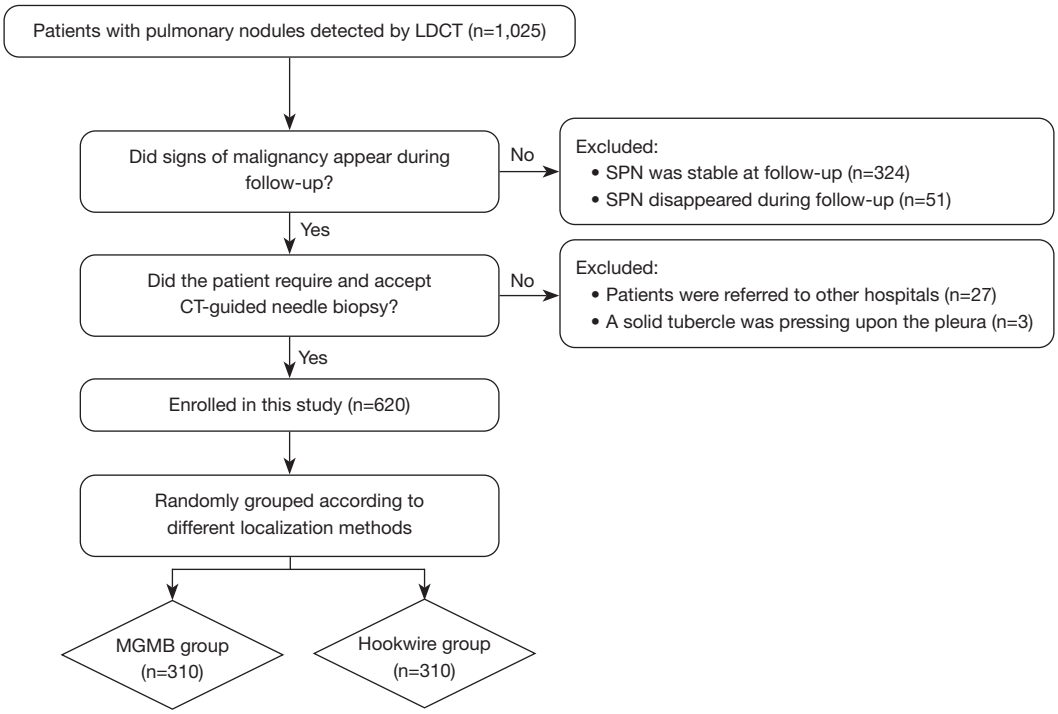


**Figure 1** Patient selection flowchart. LDCT, low-dose chest computed tomography; SPN, solitary pulmonary nodule; CT, computed tomography; MGMB, medical glue combined with methylene blue.

were females, with age ranging from 22 to 79 years (average age of 53.28±11.56 years). Due to the medical insurance policy for hospital drugs, hookwire localization was used until July 2021 and was followed by MGMB localization. In the hookwire group, there were 310 patients comprising 357 SPNs, including 269 patients with a single SPN and 41 patients with multiple SPNs (including 35 patients with 2 SPNs and 6 patients with 3 SPNs); in the MGMB group, there were 310 patients comprising 370 SPNs, including 257 patients with a single SPN and 53 patients with multiple SPNs (including 46 patients with 2 SPNs and 7 patients with 3 SPNs). Among all patients, 10 had a history of lung cancer surgery, 1 had a history of kidney cancer surgery, and 1 had a history of choriocarcinoma surgery. In contrast, SPNs in the remaining patients were discovered by physical examination or chance.

The inclusion criteria were as follows: (I) age 18–80 years; (II) pure and mixed GGNs with a maximum diameter of ≤30 mm according to CT examination; (III) imaging showing the possibility of malignant nodules (i.e., patients having a significantly larger nodule diameter or a significantly larger solid component or signs of malignancy such as lobulation or short burrs at the time of follow-up); (IV) no apparent large blood vessels, pulmonary herpes, or other essential tissue structures in the proposed puncture path; and (V) with normal coagulation function and systemic condition, able to tolerate VATS surgery, and operated upon in our hospital. Meanwhile, the exclusion criteria were the following: (I) SPN ≤3 mm mainly managed via follow-up and not resected, (II) those with pneumothorax and pleural effusion who could not complete localization, (III) the presence of multiple distant metastases within or outside the lung, (IV) the presence of contraindications to surgery (e.g., chronic obstructive pulmonary disease, severe large bullae), and (V) those with incomplete clinical or imaging data. The flowchart of patient selection is shown in *Figure 1*.

This study was reviewed and approved by the Ethics Committee of the First Affiliated Hospital of the University of Science and Technology of China (No. 2022-RE-269). Informed consent was signed by each patient and/or immediate family members before localization. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). All patient information is confidential.

 

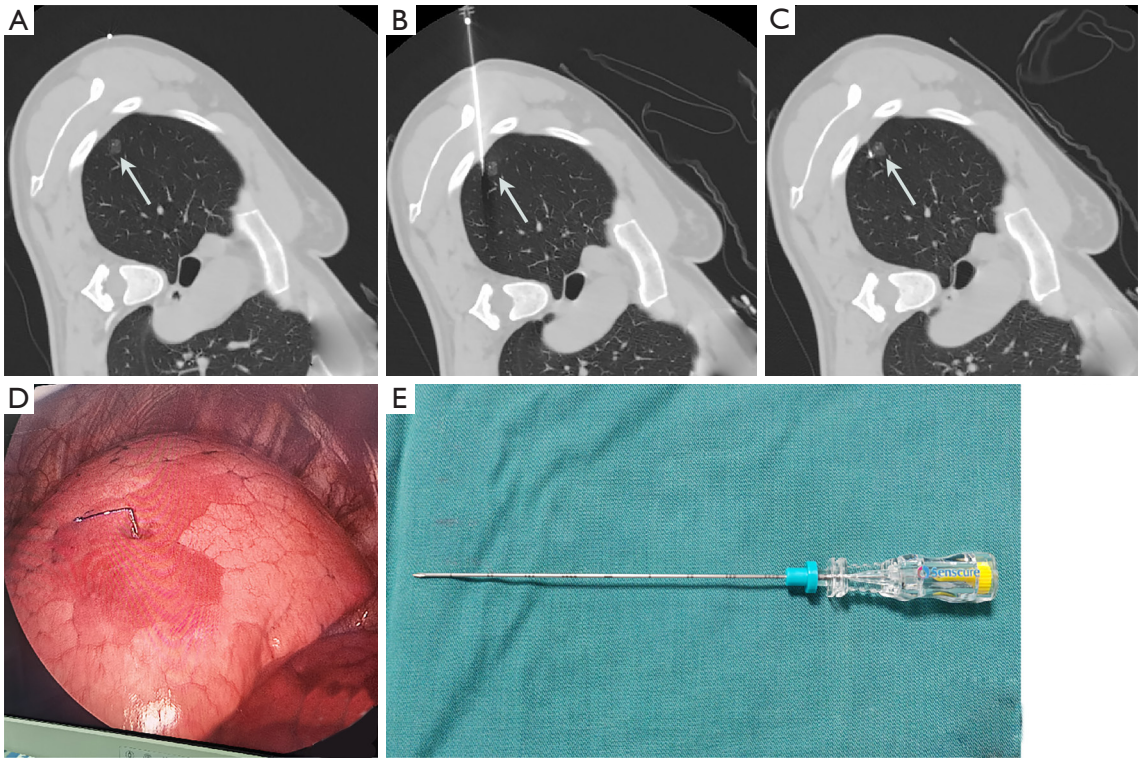


**Figure 2** A 41-year-old woman who underwent CT-guided hookwire localization of a small pulmonary nodule. (A) A nodule, approximately 1 cm in diameter, was present in the right upper lobe, with a nodule-pleura distance of approximately 0.5 cm (white arrow). (B) The tip of the needle reached within 1 cm of the nodule to release the metal anchor hook (white arrow), and the tricolor positioning wire was completely pushed out when the catheter needle was withdrawn to the soiled pleural surface. (C) Postlocalization review CT showed a metal anchor hook released approximately 0.5 cm next to the nodule (white arrow). (D) Partial wedge resection of the lung was performed, and intraoperative hookwire was seen to successfully localize the target lesion. (E) A figure of the hookwire which used in this study. CT, computed tomography.

### *Localization procedure*

The interventionist and the thoracic surgeon assessed the necessity and feasibility of each SPN localization. All patients underwent SPN localization 36 hours before VATS, which was performed by the same interventionist with 10 years of experience. First, the optimal puncture path was selected according to the size, location, and relationship between lung nodules and surrounding tissues. Next, the optimal puncture position (supine, prone, left/right position) was determined. Then, a CT scan was performed to determine the puncture needle's position, angle, and insertion depth. Finally, the puncture site was sterilized and covered with a towel, and the anesthesia was infiltrated with 2% lidocaine layer by layer.

For the hookwire group, a single-use pulmonary nodule localization needle (production approval no: 20193150175; model: SS510-10, 20 G × 100 mm) manufactured by Ningbo SensCure Biotechnology (Ningbo, China) was used, which consisted of a wire anchor hook, a push device, and a graduated puncture catheter needle. The wire anchor hook consisted of a metal anchor hook connected with a positioning wire. The hook was a nickel-titanium memory alloy wire, which could be opened as "4 claws" after release. The positioning wire was a 3-color thread of medical absorbable suture material approximately 10 cm in length. The wire anchor hook and push rod were preinstalled in the catheter needle (*Figure 2*).

For the MGMB group, a 21 G puncture needle (model: RS*A50K10SQ; 21 G × 150 mm; Terumo Medical Corporation Tokyo, Japan) was punctured to the predetermined position in steps according to the preset puncture path. First, 0.2 mL of medical tissue glue (0.5 mL; Compont, Beijing, China) was extracted with a 1-mL syringe to eliminate air. Then, 0.2 mL of methylene blue

 

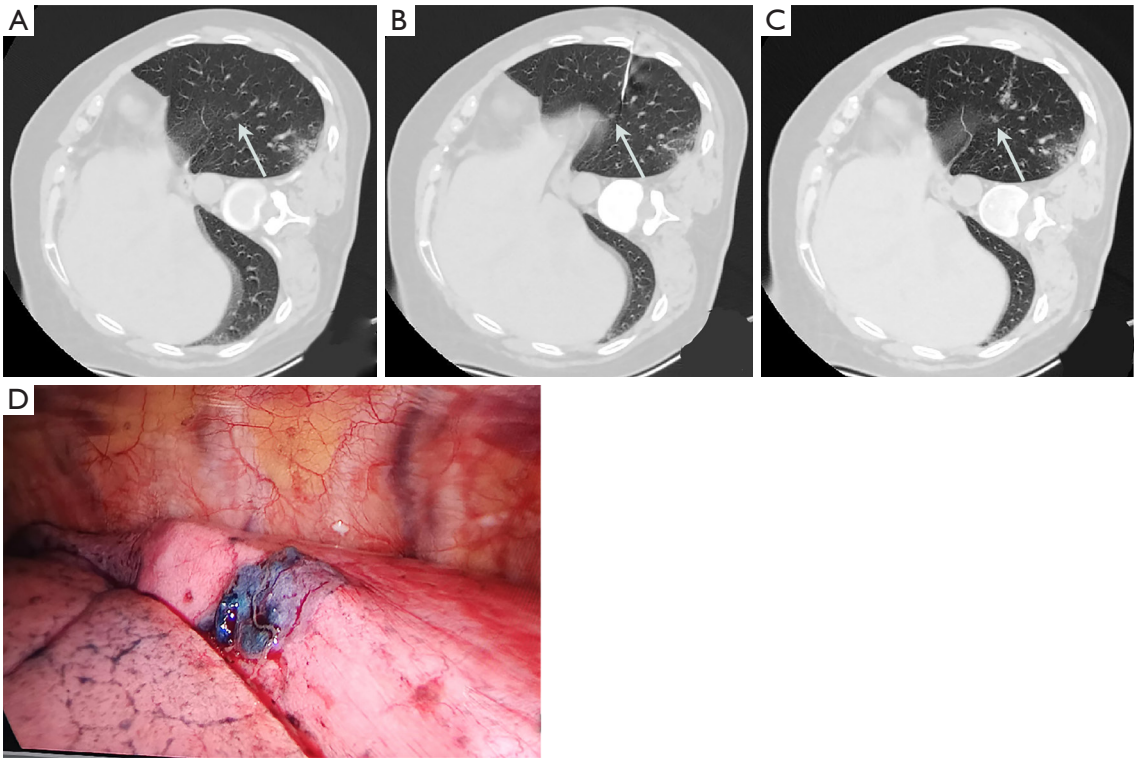


**Figure 3** A 58-year-old woman who underwent CT-guided localization of an SPN with MGMB. (A) A nodule in the left lower lobe, about 0.6 cm in diameter, with a nodule-pleura distance of approximately 4.5 cm (white arrow). (B) The tip of the needle reached the nodule at a point 1–1.5 cm near the pleural side and began injecting a mixture of medical glue and methylene blue (white arrow); a small amount of the mixture was injected while the needle was retracted until about 1 cm below the pleura. (C) After localization, another CT scan showed the formation of sclerosing glue nodules at about 1 cm next to the nodules, which was accompanied by the formation of sclerosing glue needle tracts (white arrow). (D) Intraoperative partial lung plus lymph node resection showed the blue medical glue in hard nodules. CT, computed tomography; SPN, solitary pulmonary nodule; MGMB, medical glue combined with methylene blue.

dye reagent (2 mL, Jichuan Pharmaceutical, Taixing, China) was extracted, thoroughly mixed, and quickly injected to the intended location (1–1.5 cm near the pleural side of the nodule). In case the nodule was located deeper (>3 cm from the pleura), a small amount of mixed gel (≤0.1 mL) was injected again into the subpleural area about 1 cm from the pleura after the injection around the nodule was completed. This helped to form a sclerotic nodule needle channel and avoid pleural adhesions, which aided the surgeons in finding the lesion during the thoracoscopic operation. The needle was then quickly removed after injection to avoid adhesions of the needle tip to the lung tissue (*Figure 3*).

If more than 1 nodule could not be localized in the same position, the above procedures were repeated in the appropriate position according to the priority of size, location, and imaging manifestations of suspected malignancy. In case of multiple nodules, multiple puncture needles or catheter needles were simultaneously punctured along the preset puncture path, the pleura was separately punctured, and the needle tip was pushed to the edge of the nodule. After the CT scan confirmed the needle tip position, each anchoring needle core was sequentially released, or MGMB was injected, and the catheter needle was separately withdrawn to complete localization. After localization, another CT scan of the chest was performed to confirm the location of the anchor hook or glue-sclerotic nodule and the presence of complications such as pulmonary hemorrhage and pneumothorax. The localization effects and spatial relationships between the SPNs and hookwire or MGMB were reported to the surgeon in timely fashion.

The patient was instructed to sit still for 30 min and to avoid strenuous exercise and coughing; if no abnormalities

 

were detected, the patient was returned to the ward.

### *VATS procedure*

VATS was performed under general anesthesia within 36 hours after SPN localization. Subsequently, the 2 groups underwent wedge resection after probing of the hook line of lung surface tissue and sticking glue or directly observation of the blue glue block on the lung surface for confirmation of the correct target lesions. Specimens were then collected, snap frozen, and sent for analysis; the subsequent treatment plan was devised based on the pathology results. In the case of invasive lung cancer, lobectomy plus lymph node dissection was performed according to the predetermined preoperative plan.

### *Observation indicators*

General data were collected before VATS, and the location of lesions, size of nodules, number of nodules, and nodule-pleura distance were recorded for each group of patients, as was the localization position and localization time. Localization time (measured in seconds) was defined as the time from the start of the CT scan that identified the puncture path to the end of the scan after localization was complete. The nurse who assisted in localization was responsible for calculating the localization time and recording it after the localization was completed. Complications associated with localization (such as pneumothorax, pulmonary hemorrhage, local pain, and irritating cough) were recorded in each group of patients, and the factors affecting the complications were analyzed. The localization effect was evaluated during the VATS procedure, and the inability to complete preoperative localization or to localize the target SPN intraoperatively due to the displacement of the anchor hook and the shedding of MGMB was considered a localization failure. Pathological results were recorded after VATS, and the localization-to-surgery interval and length of hospitalization were recorded for each patient.

### *Statistical analysis*

Although no formal sample size calculations were performed, as this was a retrospective study, the sample size was determined to be 310 cases in each of the 2 groups, which met the statistical criteria.

SPSS 26.0 (IBM Corporation, Armonk, NY, USA) was used for the statistical analysis. The Kolmogorov-Smirnov method was used to test whether the measurement data conformed to normal distribution. Measurement data are expressed as the mean and standard deviation (SD) if normally distributed and as the median with interquartile range (IQR) if nonnormally distributed. Comparison between 2 groups was performed using the independent samples *t*-test or Mann-Whitney test. Count data are expressed using numbers and percentages and were analyzed using the chi-squared test. Logistic regression analysis was performed for factors that may be associated with postlocalization complications. A P value <0.05 indicated statistical significance.

## Results

### *Characteristics of the patients and nodules*

The features examined in the study were summarized as patient-based (*Table 1*) and nodules based (*Table 2*), as there was more than 1 nodule in some patients. All patients underwent the pre-VATS localization procedure. The hookwire group had a 99.4% success rate (355/357), and the MGMB group had a 100% success rate (370/370). In the hookwire group, there were 125 male patients and 185 female patients, with a mean of 53.26±11.56 years (range, 22–79 years). In the MGMB group, there were 122 males and 188 females, with a mean age of 53.31±11.58 years (range, 24–78 years). There was no statistically significant differences between the 2 groups in terms of baseline information of age, gender, smoking history, number of nodules in the patients, nodule size, nodule-pleura distance, or nodule location (all P values >0.05). As for the factors during localization, the mean time of localization was significantly longer in the hookwire group than in the MGMB group (8.59±3.69 *vs.* 7.35±2.99 min; P<0.001), while the operative time was nonsignificantly longer (103.48±54.11 *vs.* 98.59±49.92 min; P=0.33). In addition, the length of hospitalization was shorter in the MGMB group than in the hookwire group (5.60±2.13 *vs.* 6.73±2.86 days; P<0.001).

### *Complications*

No death or serious complications, such as air embolism, occurred during the localization process. Complications occurred in 105 of 310 patients in the hookwire group and in 69 of 310 patients in the MGMB group (P<0.001). These

 

**Table 1** Patient-based characteristics

| Characteristics | Hookwire group (n=310) | MGMB group (n=310) | t/$\chi^2$/Z | P value |
|---|---|---|---|---|
| Age (years), mean ± SD | 53.26±11.56 | 53.31±11.58 | –0.056 | 0.95 |
| Sex, n (%) | | | 0.061 | 0.80 |
| Male | 125 (40.3) | 122 (39.4) | | |
| Female | 185 (59.7) | 188 (60.6) | | |
| Smoking history, n (%) | 86 (27.7) | 92 (29.7) | 0.284 | 0.59 |
| Number of patients with (n) | | | 1.845 | 0.39 |
| 1 nodule | 269 | 257 | | |
| 2 nodules | 35 | 46 | | |
| 3 nodules | 6 | 7 | | |
| Localization-to-surgery interval (h), mean ± SD | 17.28±5.03 | 18.66±5.14 | –4.442 | <0.001 |
| Operative time (min), median [IQR] | 90.5 [72.5] | 90 [60] | –0.967 | 0.33 |
| Length of hospitalization (days), median [IQR] | 6 [3] | 5 [3] | –5.686 | <0.001 |

t, *t*-test value; $\chi^2$, chi-squared value; Z, Z test value. MGMB, medical glue combined with methylene blue; SD, standard deviation; IQR, interquartile range.

complications were mainly pneumothorax, pulmonary hemorrhage, local pain, and irritable cough. These were mild to moderate and required no further treatment. In the hookwire group, the incidence of pneumothorax, pulmonary hemorrhage, local pain, and irritable cough was 13.5%, 9.4%, 5.8%, and 2.6%, respectively, while in the MGMB group, it was 6.1%, 3.9%, 4.5%, and 7.7%, respectively. The incidence of pneumothorax and pulmonary hemorrhage was higher in the hookwire group, while the incidence of irritating cough was higher in the MGMB group (all P values <0.05). Of note, in the hookwire group, there were 5 patients with hemoptysis and 1 patient whose aorta was damaged by a displaced anchor hook by a thoracic surgeon and had developed an aortic hematoma during surgery (*Table 3*).

### *Pathological results*

All patients completed VATS with pathological results; the main pathological findings of SPN in both groups are shown in *Table 3*. The main pathological findings in both groups were malignant lesions or glandular precursor lesions in 74.7% and 74.9%, respectively. The hookwire group included minimally invasive adenocarcinoma (n=74, 20.7%), invasive adenocarcinoma (n=49, 13.7%), adenocarcinoma *in situ* (n=59, 16.5%), and adenocarcinoma *in situ* with microinfiltration (n=85, 23.8%), while the rates of these tumors in MGMB groups were 27.8% (n=103), 17.3% (n=64), 11.1% (n=41), and 18.7% (n=69), respectively.

### *Multivariate logistic regression analysis*

Binary logistic regression analysis showed that age [odds ratio (OR) =1.040; 95% confidence interval (CI): 1.022–1.057; P<0.001], number of nodules (OR =1.624; 95% CI: 1.095–2.407; P=0.01), localization time (OR =1.086; 95% CI: 1.029–1.146; P=0.003), and localization technique (OR =0.585; 95% CI: 0.402–0.851; P=0.005) were independent factors influencing the occurrence of total complications. For pneumothorax that occurred immediately after localization, the number of nodules (OR =3.027; 95% CI: 1.878–4.879; P<0.001), localization time (OR =1.132; 95% CI: 1.058–1.212; P<0.001), and localization technique (OR =0.443; 95% CI: 0.244–0.804; P=0.007) were independent factors. For pulmonary hemorrhage, localization technique was an independent factor (OR =0.390; 95% CI: 0.195–0.780; P=0.008). For irritable cough occurring immediately after localization, localization technique (OR =3.363; 95% CI: 1.472–7.685; P=0.004), age (OR =1.502; 95% CI: 1.016–1.088; P=0.004), and nodule-pleura distance (OR =0.930; 95% CI: 0.878–0.985; P=0.01) were independent

 

**Table 2** Nodule-based characteristics

| Characteristics | Hookwire group (n=357) | MGMB group (n=370) | t/$\chi^2$/Z | P value |
|---|---|---|---|---|
| Nodule characteristics | | | | |
| Maximum diameter (mm), median [IQR] | 8 [5] | 9 [4] | –1.314 | 0.18 |
| Nodule-pleura distance (mm), median [IQR] | 10 [11] | 10 [13] | –0.601 | 0.54 |
| Lesion location, n (%) | | | 1.836 | 0.76 |
| Left upper lobe | 92 (25.8) | 108 (29.2) | | |
| Left lower lobe | 50 (14.0) | 43 (11.6) | | |
| Right upper lobe | 120 (33.6) | 127 (34.3) | | |
| Right middle lobe | 22 (6.2) | 22 (6.0) | | |
| Right lower lobe | 73 (20.4) | 70 (18.9) | | |
| Localization | | | | |
| Localization time (min), median [IQR] | 8 [4] | 7 [2] | –6.125 | <0.001 |
| Posture, n (%) | | | 40.019 | <0.001 |
| Supine position | 98 (27.5) | 52 (14.0) | | |
| Prone position | 106 (29.7) | 75 (20.3) | | |
| Left lateral position | 89 (24.9) | 149 (40.3) | | |
| Right lateral position | 64 (17.9) | 94 (25.4) | | |
| Postoperative pathological results, n (%) | | | 14.020 | 0.05 |
| Minimally invasive adenocarcinoma | 74 (20.7) | 103 (27.8) | | |
| Adenocarcinoma *in situ* with microinvasion | 85 (23.8) | 69 (18.7) | | |
| Adenocarcinoma *in situ* | 59 (16.5) | 41 (11.1) | | |
| Invasive adenocarcinoma | 49 (13.7) | 64 (17.3) | | |
| Atypical adenomatous hyperplasia | 17 (4.8) | 12 (3.2) | | |
| Inflammation | 21 (5.9) | 22 (6.0) | | |
| Alveolar epithelial hyperplasia with lymphocytic infiltration | 20 (5.6) | 29 (7.8) | | |
| Others | 32 (9.0) | 30 (8.1) | | |

t, *t*-test value; $\chi^2$, chi-squared value; Z, Z test value. MGMB, medical glue combined with methylene blue; IQR, interquartile range.

influencing factors (*Tables 4*-7).

## Discussion

Currently, VATS is considered as an effective, minimally invasive method for the clinical management of SPNs. However, failure to localize SPNs during VATS is the most common reason for conversion to open surgery (21). Therefore, safe, accurate, and effective preoperative localization of SPN is of crucial importance.

Fan *et al.* (22) developed a new disposable lung nodule localization needle (Ningbo SensCure Biotechnology, Ningbo, China), obtaining a localization success rate of 97.8% (133/136) and a localization time of 14.4±6.6 min. Lin *et al.* (19) reported the localization of SPNs through the injection of methylene blue with a localization time of 7.6±4.8 min for a single nodule. Notably, in their study, localization was not successful in 3 patients; 1 patient had extensive anthrax on the dirty pleura, making intraoperative localization challenging to discern, while in the other 2 patients, there was a rapid diffusion of methylene blue and dye spillage on the mural pleura.

 

**Table 3** Comparison of complications in the 2 groups

| Characteristics | Hookwire group (n=310) | MGMB group (n=310) | $\chi^2$ | P value |
|---|---|---|---|---|
| Pneumothorax, n (%) | 42 (13.5) | 19 (6.1) | 9.618 | 0.002 |
| Pulmonary hemorrhage, n (%) | 29 (9.4) | 12 (3.9) | 7.548 | 0.006 |
| Local pain, n (%) | 18 (5.8) | 14 (4.5) | 0.161 | 0.68 |
| Irritable cough, n (%) | 8 (2.6) | 24 (7.7) | 8.435 | 0.004 |
| Hemoptysis, n (%) | 5 (1.6) | 0 | 3.226 | 0.07 |
| Hemopneumothorax, n (%) | 2 (0.6) | 0 | 0.502 | 0.47 |
| Aortic hematoma, n (%) | 1 (0.3) | 0 | 0 | 1 |
| Total complications, n (%) | 105 (33.9) | 69 (22.3) | 10.354 | <0.001 |

$\chi^2$, chi-squared value. MGMB, medical glue combined with methylene blue.

**Table 4** Logistic regression analysis of potential risk factors for the occurrence of total complications

| Risk factor | Univariable analysis | | Multivariable analysis | |
|---|---|---|---|---|
| | OR (95% CI) | P value | OR (95% CI) | P value |
| Sex | 1.045 (0.730–1.496) | 0.81 | – | – |
| Age | 1.038 (1.021–1.055) | <0.001 | 1.040 (1.022–1.057) | <0.001 |
| Lesion location | 1.032 (0.724–1.473) | 0.86 | – | – |
| Number of nodules in the patient | 1.670 (1.143–2.441) | 0.008 | 1.624 (1.095–2.407) | 0.01 |
| Maximum diameter | 1.007 (0.960–1.057) | 0.76 | – | – |
| Nodule-pleura distance | 0.990 (0.969–1.012) | 0.37 | – | – |
| Localization time | 1.090 (1.034–1.149) | 0.001 | 1.086 (1.029–1.146) | 0.003 |
| Localization technique | 0.559 (0.391–0.798) | 0.001 | 0.585 (0.402–0.851) | 0.005 |

OR, odds ratio; CI, confidence interval.

**Table 5** Logistic regression analysis of the potential risk factors for the occurrence of pneumothorax

| Risk factor | Univariable analysis | | Multivariable analysis | |
|---|---|---|---|---|
| | OR (95% CI) | P value | OR (95% CI) | P value |
| Sex | 0.656 (0.386–1.114) | 0.11 | – | – |
| Age | 1.003 (0.980–1.026) | 0.79 | – | – |
| Lesion location | 1.044 (0.610–1.787) | 0.87 | – | – |
| Number of nodules in the patient | 2.706 (1.708–4.285) | <0.001 | 3.027 (1.878–4.879) | <0.001 |
| Maximum diameter | 0.963 (0.891–1.040) | 0.33 | – | – |
| Nodule-pleura distance | 1.010 (0.980–1.042) | 0.51 | – | – |
| Localization time | 1.140 (1.069–1.216) | <0.001 | 1.132 (1.058–1.212) | <0.001 |
| Localization technique | 0.417 (0.236–0.734) | 0.002 | 0.443 (0.244–0.804) | 0.007 |

OR, odds ratio; CI, confidence interval.

 

Recently, Wang *et al.* developed a new medical glue that can effectively accomplish localization. However, medical glues that rely exclusively on palpation for intraoperative localization are not appropriate for deeper nodules (23). Yang *et al.* demonstrated that virtual-assisted lung mapping (VAL-MAP) can be used as a complement to CT-guided localization, but a negative correlation between its marker intensity and duration indicates its inability to take a sufficiently long interval after localization, which is similar to the already proficient application of CT-guided localization (24). These localization techniques may be effective in preoperative localization but their safety needs to be further verified and a means to circumventing the limitations of the material itself should needs to be developed. Based on this clinical reality, we proposed using a combination of medical glue and methylene blue localization.

In our study, the success rate of the hookwire group was 99.4% (355/357), while that of the MGMB group was 100% (370/370), which shows that both localization techniques could be used to effectively complete preoperative localization. Complications occurred in 33.9% (105/310) of patients in the hookwire group and 22.3% (69/310) in the MGMB group (P<0.001) and included pneumothorax, pulmonary hemorrhage, local pain, and irritating cough. However, the incidence of pneumothorax and pulmonary hemorrhage was significantly higher in the hookwire group than in the MGMB group (both P values <0.05). This may be due to the thicker disposable puncture needle used for hookwire positioning (19 *vs.* 21 G), which increases the risk of gas entry during puncture. In addition, the thicker needle entering the lung parenchyma and the open "4-claw" anchor hook may also increase the risk of puncturing small vessels. On the other hand, medical glue is considered to be an ideal therapeutic adhesive material for treatment of bleeding, fistula, and gastrointestinal diseases (25,26). It also has a nontoxic and nonhazardous adhesive strength and solidifies into a hard nodule in about 5 seconds, which seals the puncture tract. Moreover, it has an important role in sticking the broken ends of blood vessels and promoting vascular contraction, as well as in promoting blood coagulation and preventing the occurrence of hemopneumothorax (23,27). The complications in this study were only mild clinical complications that did not

**Table 6** Logistic regression analysis of potential risk factors for the occurrence of pulmonary hemorrhage

| Risk factors | Univariable analysis | |
|---|---|---|
| | OR (95% CI) | P value |
| Sex | 1.876 (0.922–3.819) | 0.08 |
| Age | 1.002 (0.975–1.030) | 0.87 |
| Lesion location | 0.542 (0.286–1.027) | 0.06 |
| Number of nodules in the patient | 0.709 (0.297–1.692) | 0.43 |
| Maximum diameter | 0.981 (0.897–1.074) | 0.68 |
| Nodule-pleura distance | 0.984 (0.944–1.025) | 0.42 |
| Localization time | 1.058 (0.979–1.143) | 0.15 |
| Localization technique | 0.390 (0.195–0.780) | 0.008 |

OR, odds ratio; CI, confidence interval.

**Table 7** Logistic regression analysis of potential risk factors for the occurrence of irritable cough

| Risk factors | Univariable analysis | | Multivariable analysis | |
|---|---|---|---|---|
| | OR (95% CI) | P value | OR (95% CI) | P value |
| Sex | 0.966 (0.468–1.994) | 0.92 | – | – |
| Age | 1.047 (1.013–1.082) | 0.007 | 1.502 (1.016–1.088) | 0.004 |
| Lesion location | 2.250 (0.994–5.092) | 0.05 | – | – |
| Number of nodules in the patient | 1.449 (0.719–2.918) | 0.30 | – | – |
| Maximum diameter | 1.081 (0.992–1.177) | 0.07 | – | – |
| Nodule-pleura distance | 0.938 (0.887–0.993) | 0.02 | 0.930 (0.878–0.985) | 0.01 |
| Localization time | 0.860 (0.734–1.009) | 0.06 | – | – |
| Localization technique | 3.168 (1.400–7.166) | 0.006 | 3.363 (1.472–7.685) | 0.004 |

OR, odds ratio; CI, confidence interval.

 

require treatment.

Additionally, we found that the incidence of irritant cough was significantly higher in the MGMB group (24/310, 7.7%) than in the hookwire group (8/310, 2.6%) (P=0.004). A cough may be inevitable in patients due to the specific odor of both drugs and their possible entry into the small airways along the puncture route. However, we found that the patients' cough was temporary and tolerable. Wang *et al.* concluded that symptoms causing transient irritating cough are rare when the injection depth is <20 mm (23). Previous studies have shown that several factors may influence the occurrence of complications after localization, such as operators' experience, the size and location of SPNs, nodule-pleura distance, and patients' compliance (28,29). Our study showed a lower rate of total complications in the MGMB group ($\chi^2$=10.354; P<0.001).

The "4-clawed" hook we used reduced the incidence of displacement, yet previous studies have reported hookwire displacement in 2.5–2.7% of cases (21,27). In Xu *et al.*'s study, when the anchoring distance in the lung was <1 cm, the risk of localization failure increased (30). Not surprisingly, 2 patients in our study experienced displacement. In 1 patient, the displaced metal anchor hook damaged the aorta, after which hematoma was formed. Therefore, to reduce the time and space for anchor hook displacement, surgery should be performed as soon as possible after the completion of hookwire localization.

Our results showed that the localization-to-surgery interval was longer in the MGMB group (18.66±5.14 *vs.* 17.28±5.03 h; P<0.001), and these patients had a shorter hospitalization time (5.60±2.13 *vs.* 6.73±2.86 days; P<0.001). This may be because the sclerotic nodules formed after localization in the MGMB group were not displaced, which prolonged the time window for localization. The localization procedure was scheduled for more patients on the same day of hospitalization although they had to wait for a long time the next day before the VATS procedure. They were discharged one day earlier than the patients in the hookwire group, which shortened the average length of stay, accelerated bed availability, and served more patients in need of VATS surgery. Therefore, MGMB localization has greater potential clinical value.

Our experience in the localization of 620 patients has provided certain insights into these procedures. First, during hookwire localization, for SPNs closer to the pleura (<1 cm), the anchor hook should be released along the nodule location's longitude, ensuring a sufficiently long intrapulmonary anchoring distance and reducing the occurrence of displacement. Second, during MGMB localization, for deeper SPNs (>3 cm), a small amount of mixed glue (about 0.1 mL) can be injected while the needle is being retreated after the injection around the nodule is completed, up to a position of about 1 cm from the pleura to form a sclerosing glue needle channel. In this way, even if the surgeon cannot palpate a deep hard nodule during surgery, it is still possible to determine the location by observing the dye on the lung surface or pleural wrinkling. Third, for preoperative localization of multiple nodules in the ipsilateral lung, once pneumothorax occurs in the first nodule during localization, it seriously interferes with the accuracy of localization of other nodules in the ipsilateral lung. Therefore, we tend to perform simultaneous punctures with multiple catheter needles along the preset puncture path, puncturing the pleura and then pushing the needle tip to the edge of the SPN to release the anchor hook or inject MGMB.

There are some limitations to this study. First, given its retrospective study, there may be patient-related selection bias. Second, all patients were from a single hospital, and the sample size was not very large. Future multicenter studies with larger sample sizes will help to improve the credibility and persuasiveness of the results. Finally, we did not conduct further classified studies on the location, size, or distance from the pleura of patients' SPNs. Whether different types of nodules would have different results is worthy of further study.

In conclusion, both localization techniques can efficiently accomplish the preoperative localization of SPNs; therefore, either could be preferred depending on the economic costs, infrastructure, experience of the performing physician, and other factors. Nonetheless, compared with hookwire method, MGMB involves fewer complications and a lower incidence of complications and is thus worthy of clinical promotion.

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## Footnote

*Reporting Checklist*: The authors have completed the

 

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*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-22-1240/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. This study was reviewed and approved by the Ethics Committee of the First Affiliated Hospital of the University of Science and Technology of China (No. 2022-RE-269). Informed consent was signed by the patients and/or immediate family members before localization. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).



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