Journal of Cardiothoracic Surgery

RESEARCH

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The efficacy of the 4-hook needle localization for pulmonary ground glass nodules: a single-center retrospective analysis

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Abstract

Introduction The aim of this study was to evaluate the efficacy of the 4-hook needle localization for pulmonary ground glass nodules (GGNs).

Methods From November 1, 2021, to May 31, 2024, 194 patients were diagnosed with one or more GGNs by computed tomography (CT) scan and underwent preoperative CT-guided 4-hook needle localization followed by video-assisted thoracoscope surgery (VATS) wedge resection, segmentectomy or lobectomy. There were 226 nodules in all patients. We analyzed the 4-hook needle localization safety, complications, safe margin and localization depth.

Results The 4-hook needle localizations success rate was 100% and didn't take place in displacement and dislodgment. The tumor margin distance is about 5–20 mm and all tumor margin was negative thorough final pathology result. 9 patients occurred small parenchymal hemorrhage, 13 patients occurred small pneumothorax and 8 patients occurred small hemoptysis, those complications needn't intervene or tackle and didn't affect surgery. Compared upper and middle lobe to lower lobe, localization time was 13.92 ± 4.6 min vs 13.66 ± 4.28 min respectively, $p = 0.69$, there was no significant statistical difference. Localization depth was 18.63 ± 7.8 mm vs 15.87 ± 8.52 mm respectively, $p = 0.02$, there were statistical differences, but the margin tumor distance was 5.16 ± 4.94 mm vs 4.93 ± 3.64 mm, $p = 0.73$ respectively, there was no statistical difference.

Conclusions Preoperative 4-hook needle localization is safe and feasible for GGNs. Guided by 4-hook needle localization, wedge resection can ensure enough safe margins and patient was well tolerated.

Keywords 4-hook needle, Localization preoperative, GGNs, Video-assisted thoracoscopy surgery, Wedge resection

Introduction

Lung cancer is the leading cause of deaths among cancer patients around the world [1]. The detection rate of GGNs has increased year by year, especially in young people or female non-smoking, has a high proportion of malignances [2, 3]. The malignant proportion of GGNs accounted for a rate of 87.2% [4]. Although GGNs as an indolent subtype of lung adenocarcinoma, it requires special management [5].

Malignant GGNs are important to regular follow up or intervention, earlier intervention as an active method can improve survival rates, surgical treatment is the first choice [6]. Fu et al. illustrated that the 5-year recurrence-free survival (RFS) with purify GGNs (pGGNs) and mix GGNs (mGGNs), stage I was 100% VS 87.6% [7]. Atypical adenomatous hyperplasia(AAH), carcinoma in situ(AIS), minimally invasive adenocarcinoma(MIA) were classified together as a low-risk group, the 5-year RFS rate was

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also 100% [8]. Tsutani et al. reported patients with clinical stage IA lung adenocarcinoma with more than 50% GGNs component, there was no statistically differences in 3-year RFS undergoing lobectomy (96.4%), segmentectomy (96.1%), or wedge resection (98.7%) [9]. The 5-year RFS rate of partial lung resection for GGN dominant lesions with a consolidation tumor ratio < 0.25 was 99.7% [10]. Wedge resection is suitable for the most patients with GGNs and is curative [11].

GGNs depend on direct visualization or palpation intraoperative in past. Small, purify or deep GGNs are often difficult to palpate or identify during VATS, which extends operation time and increase normal lung tissue damage. Moreover, the safety margin of GGNs can't be accurately predicted and even miss GGNs [12, 13]. Surgery needs to remove little lung tissue and doesn't shorten RFS and overall survival (OS). At present, preoperative CT-guided localization is a good choice, 4-hook needle as a novel GGNs localization device, has been reported in clinical studies [14].The aim of this study was to evaluate the efficacy of the 4-hook needle localization in patients with VATS.

Materials and methods

This retrospective study was performed in accordance with the principles outlined in the Declaration of Helsinki and approved by the Ethics Committee of The Third Affiliated Hospital of Sun Yat-Sen University (No. II2024-094–01). Informed consent was obtained from all patients before preoperative 4-hook needle localization as well as the utilization of their personal data. The study was received approval.

Patients and inclusion criteria

This was a single-center retrospective study. From November 1, 2021, to May 31, 2024, data from 194 patients who were diagnosed with one or more GGNs by CT scan, all GGNs for localization and resection were suspicious for malignancy at first. There were 226 nodules in all patients. we collected all patients' materials via the electronic medical record system in the third affiliated hospital of Sun Yat-Sen University.

The eligible criteria for GGNs wedge resection included in: (I) GGNs with a maximum transverse diameter of ≥ 8 mm but ≤ 20 mm, and with a solid component < 5 mm or solid part is < 20%; According to the current agreements and 2023 guideline from the American Cancer Society, diameter of ≥ 8 mm GGN can be treated with surgery, and smaller GGN should be regular follow-up [15]. (II) enlargement or density increase of GGNs during regular follow-up by CT scan; (III) isolated lung metastasis when the primary tumor was cured or well controlled; (IV) ipsilateral multiple nodules which was same suspected to be malignant and < 8 mm in size, were synchronously localized and resected, and (V) the depth from pleural of GGNs is ≤ 30 mm. The CT parameters of nodules were examined in lung window settings (window level: − 500 HU, window width: 1500 HU) by two researchers. Clinical characteristics are shown in Table 1.

Table 1 Clinical characteristics of patients and GGNs

Variables	Value (N1 = 194, N2 = 226)
Gender	
Male	79(40.4)
Female	115(59.6)
Age (years)	51[16–81]
Smoker	
Yes	49(25.4%)
No	145(74.6%)
Nodule type	
Pure GGN	130
Part-solid	73
Solid	23
Location of nodule	
Left upper lobe	47
Left lower lobe	37
Right upper lobe	95
Right middle lobe	9
Right lower lobe	38
Nodule size (diameter mm)	9.7[4–20]
Nodule depth* (mm)	
Depth < 20	158
Depth > 20	68
Tumor margin distancer(mm)	10.4[5–20]
Pathological diagnosis	
AAH	5
AIS	51
MIA	119
IAC	15
Metastatic tumor	8
Others**	28
Stage***	
Benign	33
0	51
IA1	134
IV(metastatic tumor)	8

Values are presented as median [range] or n (%)

N1, number of patients. N2, number of GGNs

* nodule depth was defined as the distance between the nearest visceral pleural surface and the nodular inner margin

** including inflammation, granuloma, benign tumor and lymph node

*** stage was determined by the eighth edition classification of lung cancer

Interventional equipment and localization techniques

A 64-slice helical CT scanner (layer thickness 1.25 mm) was used to guide percutaneous puncture and localization. 4-hook needle with a scaled suture (Sheng Jie Kang Biological Technology Co., Ltd., Ningbo, China) was used for localization. The localization device contains a 4-hook anchor and a tricolored suture with a scale. Anchor can fix in lung tissue and tricolored suture could evaluate the depth of localizations (Fig. 1).

The puncture route was determined by the location and adjacency of nodule and adjusted according to the planned VATS approach. Usually, the puncture route was the shortest distance to the pleura and the least amount of lung tissue traversed as possible. Target position of the 4-hook needle was localized behind or beside the nodule within 10 mm, but not the surface visceral pleura or in front of nodule, then to estimate the depth of nodules. After claw released, the patient was taken a final CT scan to confirm the device position and any complications (Fig. 2). Then patients returned to the ward and underwent the operation next day usually.

Surgical procedure

Patients were placed under general anesthesia via a laryngeal mask, single-lumen endotracheal tube or double-lumen endotracheal tube after the assessment of the anesthesiologist and surgeon. According to difficulty of operation, nodules position, skills of surgeon, the single port or 2-ports VATS was used. Single port about 3 cm in the fourth or fifth intercostal space was made at the anterior axillary line. If 2-ports method, another port about 1 cm in the seventh intercostal space was made at the midaxillary line for the thoracoscope. The patient's breathing was resumed with a small tidal volume (about 250 ml) and high frequency (about 18 times per minute). When entering the thoracic cavity, patient's breathing was stopped for a little while. The lung tissue was compressed by an oval forceps to make the lung collapsed

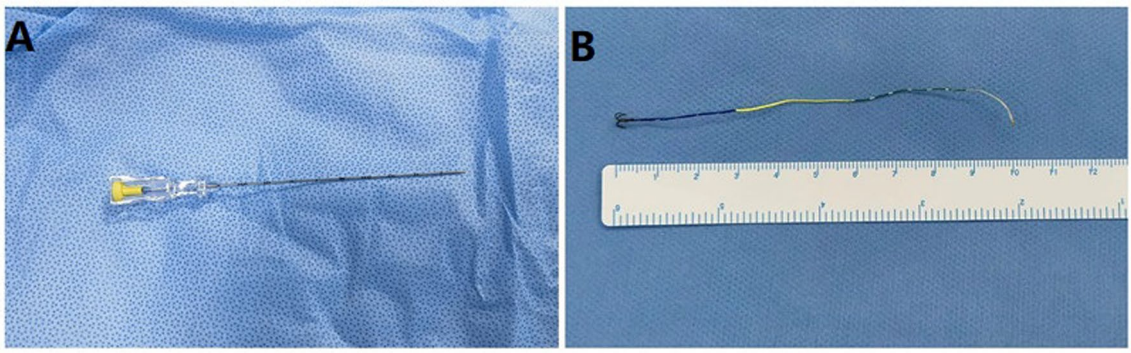

Fig. 1 **A** The 4-hook needle, **B** The 4-hook anchor and a tricolored suture with a scale

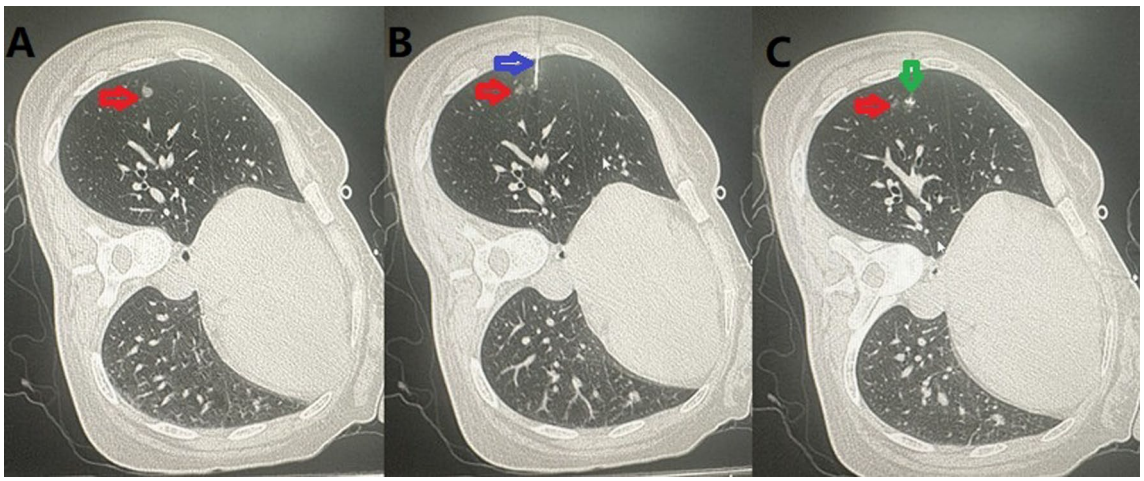

Fig. 2 Localization nodule: the red arrow; 4-hook needle: the blue arrow; 4-hook needle claw: the green arrow. The procedure for 4-hook needle localization nodule: **A**: patient is positioned appropriately, and the location of the nodule is determined by CT scan. **B**: a puncture needle is used for target nodule localization; **C**: the 4-hook needle claw is released and fixed to lung tissue

completely. The tri-colored suture on the surface of the pleura was found easily.

Wedge resection steps were as follows: First, the scale suture was gently lifted to determine the depth of the claw. Second, the visceral pleura and scale suture were pulled by a curved forceps, then an oval forceps (diameter of about 1 cm) was used to evaluate the resection margin. The expected resection margin distance was evaluated by the diameter of nodule, the reading of scale suture and the location relationship between anchor and nodule and was equal to the diameter of nodule at least. Subsequently, the resection margin was marked. Finally, both the nodule and anchor were resected completely with staplers along the marked line (Fig. 3).

The specimen was incised along the maximum diameter of nodule and perpendicular to the stapler line, and the resection margin distance, from the nodule's inner border to the nearest staple line, was measured with a ruler in its natural state and recorded in the surgical record. Then frozen pathologic examination was performed. Complete resection is sufficient if the disease is benign or metastatic, regardless of the resection margin distance. The resection saft margin distance is required to be ≥ 5 mm if the disease is carcinoma in situ or malignant according to the JCOG 0804 study. An expanded wedge resection is required if the resection margin distance is < 5 mm in case of IAC, while segmental or lobectomy is performed if an extended wedge resection is impracticable.

Histopathological evaluations

The tumor margin distance was measured macroscopically which was defined as the shortest width between the resection line. All nodules and the margin tissue were examined by histologically. According to the 2015 World Health Organization (WHO) Classification of Lung Tumors, MIA and AIS were defined as small (≤ 3 cm) solitary adenocarcinomas that exhibited a lepidic growth pattern with ≤ 5 mm invasion (MIA) or without invasion (AIS) respectively.

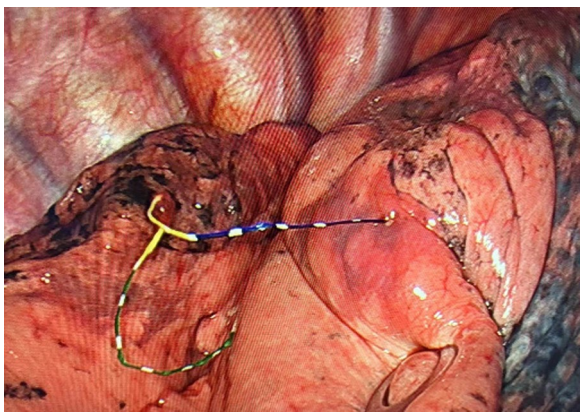

Fig. 3 Intraoperative VATS showed the tri-colored suture on the surface of the pleura and the 4-hook claw fixed to lung tissue

Main observation indicators

The main indicators include the nodules position, diameter, depth, and the distance between the claw and nodule, localization time, success rate of localization, complications and resection tumor margin distance. The depth of the nodule was defined as the distance between the nearest visceral pleural surface and the nodule's inner border. Successful localization was defined no dislodgement or displacement. All the indicators were determined and recorded by two researchers after they reached a consensus.

Statistical analysis

SPSS version 20.0 (IBM Corp., Armonk, NY, USA) used for the statistical analyses. Quantitative variables were expressed as a number, median, and range, and categorical variables were described as a number and percentage. The descriptive statistics were presented as mean ± SD. Categorical variables were assessed using Mann–Whitney U tests. A p value < 0.05 was considered to indicate a statistically significant difference.

Results

Baseline statistics

Totally 194 patients (79 male and 115 female; median age, 51 years; age range, 16–81 years) with 226 GGNs were involved, who underwent CT-guided 4-hook needle localization and then carried out wedge resection, segmentectomy or lobectomy with VATS. All 226 nodules were successfully resected with pathological negative margins. pGGNs, mGGNs and sGGNs were 130 nodules,73 nodules and 23 nodules respectively. GGNs diameter was 4–20 mm an margin distance was 5–20 mm. The nodules distance to the pleural surface less than 20 mm were 158 and more than 20 mm were 68. 47 nodules located in left upper lobe, 37 nodules located in left lower lobe, 95 nodules located in right upper lobe, 9 nodules located in right middle lobe and 38 nodules located in right lower lobe. The final pathological diagnosis included in AAH 5 nodules, AIS 51 nodules, MIA 119 nodules, IAC 15 nodules, metastasis tumor 8 nodules and others benign nodules 28. (Table 1).

Localization and surgical procedure outcomes

There were no major complications or deaths perioperative. 57 nodules with the depth of anchor claw were less than 10 mm, 101 nodules were 10 mm and 20 mm; 60 nodules were 20 mm and 30 mm and the other 8 nodules

were more the 30 mm. The anchor claw was placed in 4 nodules and around 222 nodules, 174 anchor claws placed within 10 mm around nodules and 48 anchor claws placed more than 10 mm.The localizations success rate was 100%. 168 patients with single nodule, 20 patients with 2 nodules and 6 patients with 3 nodules underwent simultaneous localization and resection.

Complications included parenchymal hemorrhage was 9 patients, asymptomatic pneumothorax was 13 patients and hemoptysis was 8 patients. Those complications were small and needn't special medical intervention. We didn't use hemostatic drugs or place thoracic drainage, and monitored vital signs. Blood pressure, heart rate and blood oxygen saturation were normal. There was no cases of dislodgement or claw-suture fracture during the entire process. All devices were visualized at the first attempt before VATS resection and retrieved entirely with the resected nodules (Table 2).

Compared upper and middle lobe to lower lobe, localization time were 13.92 ± 4.6 min vs 13.66 ± 4.28 min respectively, $p = 0.69$, there was no statistical difference. Location depth was 18.63 ± 7.8 mm vs 15.87 ± 8.52 mm respectively, p = 0.02, there were statistical differences in two group. The margin safe distance were 5.16 ± 4.94 mm vs 4.93 ± 3.64 mm, $p = 0.73$, there was no statistical difference between the two groups. Data analysis is shown in Table 3.

Table 2 Outcome of localization and surgery

Variables	N
The depth of the anchor claw* (mm) (nodules)	
Distance ≤ 10	57
10 ≤ distance ≤ 20	101
20 ≤ distance ≤ 30	60
Distancer > 30	8
Location of the anchor claw(mm) (nodules)	
In nodules	4
Around nodules	222
1 < distance ≤ 10	174
Distance > 10	48
Localization related complications (patients)	
Parenchymal hemorrhage	
Small	9
Large	0
Pneumothorax	
Small (no symptoms)	13
Large	0
Hemothorax	0
Hemoptysis (small)	8
Retrieve of device after resection	226

N, the number of GGNs or patients

* the depth of the anchor claw was defined as the distance between the nearest visceral pleural surface and inner margin of the anchor claw

Discussion

GGNs between 5–10 mm should performed LDCT in first 6 months followed by annual LDCT for 2 years or resection when developed solid part or increased in size. GGN > 10 mm, LDCT should be done in 3–6 months regular followed by LDCT in 6–12 months or biopsy or resection [4]. GGNs increase anxiety and nervous in most patients, VATS is a major therapy and/or diagnosis method in GGNs which especially first considered the malignances.

Accurate localization for GGNs are an essential step in resection and also avoid unnecessary extensive resections [16]. Hook-wire, coil, indocyanine green (ICG), Virtual-assisted lung mapping (VAL-MAP), ultrasound and 4-hook needle methods were usually used to preoperative or intraoperative localization [17–19]. The pneumothorax rate in patients undergoing the Hook-wire localization was the 33–38% rates reported previously [20], resulted in poor experience and more pain. ICG overflow and diffusion in the chest cavity would result in localization failure and multiple GGNs isn't possible successful. Surgery is required within 3 h after localization, its fluorescence signal has a limited depth and can't detect deeper GGNs [21]. VAL-MAP as a localization method, its procedure requires multiple steps and is difficult to perform in many hospitals; Second, it isn't possible to confirm the mapping points preoperatively [22].

4-hook needle as a novel device, which located success rate was 100% and didn't take place in displacement and dislodgment intraoperative. It stays in patient body relatively longer and have lower VAS scores, discomfort and complications, only a few patients need painkiller. The 4-hook needle claw have a strong binding force with the lung tissue and the position is relatively fixed, its posterior connection is a soft line, which can reduce the stimulation of pleura, especially multiple GGNs [13]. Otherwise, operator can obviously palpate or observe the 4-hook needle and easily determine the nodules position by judging the localization.

Localization complications are usual pneumothorax and hemorrhage, including in 9 patients occurred small

Table 3 Data analysis of upper and middle lobe vs lower lobe

	Upper and middle lobe	Lower lobe	*p* value
Localization time (min)	13.92 ± 4.6	13.66 ± 4.28	0.69
Location depth of the claw(mm)	18.63 ± 7.8	15.87 ± 8.52	0.02
Margin distance (mm)	5.16 ± 4.94	4.93 ± 3.64	0.73

parenchymal hemorrhage, 13 patients occurred small pneumothorax, 8 patients occurred small hemoptysis, those complications needn't intervene or tackle. The pneumothorax rate is 6.7% in our study, is lower than Hook-wire localization [20]. Those complications don't affect and delay surgery, patients recover successfully and without any new complications or sequelae, which demonstrated that the 4-hook needle method was safe.

GGNs with a diameter < 20 mm could be managed with sublobectomy [23–25]. Wedge resection was related to fewer complications, lower risk and preserved more lung tissue [26]. All GGNs were first performed wedge resection. Frozen results indicated 15 patients with IAC, which 10 patients didn't perform lobectomy or segmentectomy due to poor lung function and 5 patients underwent lobectomy or segmentectomy. IAC with margins < 5 mm, we performed lobectomy or segmentectomy for patients according to diameter, consolidation-to-tumor ratio (C/T) and lung function. JCOG0802/WJOG4607L showed that peripheral GGNs with a diameter ≤ 2 cm improved OS after segmentectomy compared with lobectomy [27]. GGNs with a diameter > 3 cm performed lobectomy [28].

Enough margin distance plays a role in wedge resection, which contributes to survival and recurrence for early NSCLC. Wolf et al. found that the tumor margin distance > 9 mm was associated with the improved RFS, and tumor margin distance > 11 mm was associated with improved OS [29].The tumor margin distance is 5–20 mm in our study. Operator can better locate the tumor margin distance by the 4-hook needle mark. The margin was negative in all patients thorough final pathology result.

Compared upper and middle lobe to lower lobe, location depth was statistical differences, but margin distance was no statistical difference in two group. On the one hand, the nodules of lower lobe are perhaps close to the pleura; on the other hand, due to the influence of breathing, lower lobe has large motion and the localization isn't deep. No matter the nodule location, the 4-hook needle can guide surgery, ensure to resect all nodules successfully and have enough negative margin.

Multiple GGNs are becoming more and common, which are usually considered multiple primary lung carcinomas [30]. All 20 patients with 2 nodules and 6 patients with 3 nodules underwent simultaneous localization and resection. Multiple nodules localizations can reduce stimulation of pleura and decrease the incidence of pneumothorax and hemorrhage by the 4-hook needle. Otherwise, one nodule removed first and the other nodules are difficult to locate due to anatomical changes in the same lobe, 4-hook needle localization can help to remove the target nodules and preserve more lung tissue. For patients with 2 or 3 GGNs, the localization time in every GGNs was almost the same as the single-nodule, those patients' complication rates weren't higher than the single-nodule localizations.

Nodule location deeper than 30 mm from the pleura, although the 4-hook need localization, it is difficult to perform wedge resection in some lung lobe, which doesn't ensure enough margins, deep GGNs usually perform segmentectomy or lobectomy. In older patients with multiple comorbidities and poor lung function, nonsurgical treatment is available for GGNs. Stereotactic body radiotherapy (SBRT) and Radiofrequency ablation (RFA) are alternative treatment as treatment for GGNs [31].

There are some limitations in our study. First, we only admit a small number of patients and this study is a single-center retrospective study, which it lacks large multicenter, randomized controlled trials to support. Second, the longest follow-up time was 2.5 years at present in all patient for malignant GGNs, no one had tumor recurrence and all survived, whether 4-hook needle localization promoting recurrence or metastases needed further follow-up and research.

Conclusion

Preoperative CT-guided 4-hook needle localization for VATS is safety and feasible in GGNs. It can stay in patient body relatively longer, reduce the operation difficulty, improve the success rate and has a low complications rate. Guided by 4-hook needle localization, wedge resection can ensure enough tumor margins. It is a recommended localization method for GGNs.

Abbreviations

GGN	Ground glass nodule
CT	Computed tomography
VATS	Video-assisted thoracoscope surgery
LDCT	Low dose CT
HRCT	High-resolution CT
RFS	Recurrence-free survival
pGGNs	Purify GGNs
mGGNs	Mix GGNs
AAH	Atypical adenomatous hyperplasia
AIS	Carcinoma in situ
MIA	Minimally invasive adenocarcinoma
OS	Overall survival
IAC	Invasive adenocarcinoma
ICG	Indocyanine green
VAL-MAP	Virtual-assisted lung mapping
SBRT	Stereotactic body radiotherapy
RFA	Radiofrequency ablation

Acknowledgements

No

Author contributions

ZJ and CHG designed this work. WYH, ZK and XJN collected the clinical data. HYH performed the statistical analyses. WYH wrote this article. Final manuscript was approved by all authors.

Funding
None.

Availability of data and materials
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval
This retrospective study was performed in accordance with the principles outlined in the Declaration of Helsinki and approved by the Ethics Committee of The Third Affiliated Hospital of Sun Yat-Sen University (No. II2024-094–01). Informed consent was obtained from all patients before preoperative 4-hook needle localization as well as the utilization of their personal data. The study was received approval.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 16 October 2024 Accepted: 8 February 2025
Published online: 06 March 2025

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