The application value of computed tomography in combination with intraoperative noninvasive percutaneous ultrasonic localisation of subpleural pulmonary nodules/ground-glass opacity in uniportal video-assisted thoracoscopic surgery

Qi Zhang, Zhiqiang Wang, Yuequan Jiang, Fang Li, Zhi Zhang, Huarong Cai
Chongqing Key Laboratory of Translational Research for Cancer Metastasis and Individualized Treatment, Chongqing University Cancer Hospital, Chongqing, China

Abstract

Introduction: This study investigates the application value of preoperative noninvasive computed tomography (CT) localisation, combined with intraoperative percutaneous ultrasonic localisation, in the precise positioning and excision of subpleural pulmonary nodules/ground-glass opacity in uniportal video-assisted thoracoscopic surgery (U-VATS).

Aim: To derive the precise positioning and excision of subpleural pulmonary nodules by CT combined with intraoperative percutaneous ultrasonic localisation and to avoid the complications caused by preoperative CT-guided puncture localisation, reduce physiological and psychological stress such as anxiety, CT radiation dose, and treatment cost, and to improve the treatment satisfaction of patients.

Material and methods: A total of 54 patients with subpleural pulmonary nodules/ground-glass opacity (SPN/GGO), who were treated in our hospital from June 2017 to January 2020, were enrolled in this study. The patients were randomly divided into a treatment group (n = 23), and the nodules were scanned by high-resolution CT and marked at the shortest distance on the surface of the body prior to surgery. These pulmonary nodules were relocated by ultrasound at the original CT positioning points in the same body position following the administration of general anaesthesia. Then, the hookwire puncture location was performed under real-time guidance. For the control group (n = 31), the subpleural pulmonary nodules were located by CT-guided puncture and embedding a hookwire prior to surgery. Pulmonary wedge resection was performed by U-VATS in each group. The subpleural nodules were confirmed by the naked eye and rapid pathological diagnosis after surgery. The difference in positioning success rate, positioning time, the incidence of complications, and patient anxiety scores for subpleural pulmonary nodules were compared and analysed between the two groups.

Results: A total of 22 cases of subpleural nodules were successfully located in the treatment group at a success rate of 95.6% (22/23). The average positioning time for CT in combination with ultrasound was 22.0 ± 5.9 min. In the control group, 31 cases of subpleural pulmonary nodules were satisfactorily located at a success rate of 100% (31/31). The average positioning time of CT was 24.2 ± 5.4 min. The difference in positioning success rate and positioning time was not statistically significant (p = 0.24; p = 0.15) between the two groups. The incidence of complications and SAS anxiety scores in the treatment group were lower compared with the control group. The difference was statistically significant (p = 0.002; p < 0.001).
Conclusions: Preoperative CT combined with intraoperative percutaneous real-time noninvasive ultrasonic localisation can accurately locate subpleural pulmonary nodules, with a high degree of safety and good tolerance in patients who are suitable for U-VATS.

Key words: high-resolution computed tomography, percutaneous real-time ultrasound, subpleural pulmonary nodules, uniport video-assisted thoracoscopic surgery.

Introduction

Lung cancer is one of the most malignant among cancerous tumours with the highest morbidity and mortality [1]. In recent years, with the enhancement of people’s general health awareness and the application of high-resolution computed tomography (CT) [2], ground-glass opacity (GGO) and solid pulmonary nodules (SPN) can be detected in time. Many of these cases represent early lung cancer or precancerous lesions, where the likelihood of GGO malignancy can be as high as 59–73% [3]. Thoracoscopic surgery is the preferred option for GGO and pulmonary oligometastatic foci. As a type of peripheral pulmonary nodules, subpleural pulmonary nodules are superficial in terms of location. These nodules are small; in particular, the characteristics of GGO foci closely resemble the pulmonary parenchyma and can thus be difficult to detect by finger palpation during surgery [4]. If a subpleural nodule is located at the back of the thorax or at a distance from the surgical incision, even in cases where it is solid or sub-solid, it will be difficult to palpate when using uniportal thoracoscopy. This will result in the prolongation of surgery time, an increase in incisions, conversion to thoracotomy, and even the expansion of the scope of resection. In addition, the complications of a preoperative puncture location can render patients anxious about puncture, leading to a poor perioperative treatment experience. Therefore, accurate localisation and complete resection of pulmonary nodules represent challenging tasks for thoracic surgeons.

Aim

The purpose of this study is to derive the precise positioning and excision of subpleural pulmonary nodules by CT combined with intraoperative percutaneous ultrasonic localisation and to avoid the complications caused by preoperative CT puncture localisation, reduce physiological and psychological stress such as anxiety, the CT radiation dose, and treatment cost, and to improve the treatment satisfaction of patients.

Material and methods

Clinical material

A total of 54 patients with subpleural pulmonary nodules admitted to our hospital from June 2017 to January 2020 were enrolled in the study. All patients were admitted to the hospital for a high-resolution CT scan. Inclusion criteria were as follows: nodules were no further than 10 mm from the pleura. Exclusion criteria were as follows: patients with nodules completely covered by rib or scapula, pleural thickening, or pleural adhesion. Participants were randomly divided into the following groups: 1) a treatment group (n = 23) receiving preoperative CT in combination with intraoperative percutaneous real-time ultrasonic localisation; 2) a control group (n = 31) receiving preoperative CT-guided puncture. Hookwire puncture localisation was adopted in both groups, and U-VATS Pulmonary wedge resection was the preferred option for all nodules.

According to the diagnosis and treatment guidelines for pulmonary nodules, the surgery indications were met and there were no surgery-related contraindications. Participants provided informed consent for their participation in the study prior to undergoing surgery.

Instruments and equipment

High-resolution CT (Somatom GO-UP, Siemens Healthcare, Munich, Germany) was performed with parameters as follows: tube voltage = 130 kV, tube current = 56 mA/s, increment collimation = 16 × 0.75 mm, pitch = 1.5, rotation time = 0.5 s. The reconstruction parameters were as follows: slice thickness = 1.5 mm, increment = 1.2 mm, soft-tissue convolution kernel (Br40) and lung convolution kernel (B60), field of view = 400 × 400 mm, matrix: 512 × 512. Ultrasound (Sonoscape Color Doppler ultrasonic diagnosis apparatus) was performed. The ultrasonic probe model was a Canon Convex Array Transducer, model PVT-375BT; Canon Linear Array Transducer, Model PLT-1005BT. Equipment parame-
The application value of computed tomography in combination with intraoperative noninvasive percutaneous ultrasonic localisation of subpleural pulmonary nodules/ground-glass opacity in uniportal video-assisted thoracoscopy

Material and methods

Preoperative computed tomography body surface location labelling method

High-resolution, CT was used to locate the nodules one day prior to surgery or on the day of surgery. According to the surgery position, the patient was placed in a 90° lateral position. The affected upper limb extended towards the head and the hands were laced behind the patient’s head. A body surface positioning grid was placed near the nodule, and the location of the nodule was determined by CT scanning. The nodule located closest to the positioning grid was picked up. The best puncture position was adopted as the intersection point between the positioning grid and the infrared ray and was marked (in blue) on the surface of the body, waiting for the surgery.

Intraoperative ultrasound-guided percutaneous puncture and localisation

Following successful double-lumen endotracheal intubation under general anaesthesia, the patient was placed in the same body position. The pulmonary nodule (red) was again located near the CT positioning point. When the location of the subpleural nodule was displayed on the ultrasound, the hookwire puncture was performed under real-time guidance to localise the nodule within 1 cm, and the needle tip was located 2 cm deep into the nodule. The formation of the pneumothorax was evaluated by ultrasound following the puncture. The external puncture needle was cut through. All patients were operated on by the same sonographer.

Statistical analysis

The age, positioning time, and SAS anxiety scores were compared between the two groups using...
a $t$-test. Gender, positioning success rate, and complication rate were compared by $\chi^2$ test. Fisher’s precise test was used for positioning nodules; $p < 0.05$ suggested a statistically significant difference.

**Results**

The experimental group included seven male and 16 female participants, with an average age of 46.5 ±22.3 years. The distribution of SPN/GGO was as follows: pure GGO (pGGO, a slight increase in the density of shaded or round nodules found in CT. Because the texture of the bronchi and blood vessels inside it can still be displayed, this situation looks very similar to ground glass.), $n = 4$; mixed GGO (mGGO, a mixed density ground glass opacity, which is the solid components in pGGO with uneven density.), $n = 14$; and SPN, $n = 5$. There were 17 cases involving the right lung and 6 cases involving the left lung. The mean size of the nodules was 11.4 ±6.3 mm. The control group included nine males and 22 females with an average age of 50.1 ±18.6 years. The distribution of SPN/GGO was as follows: pGGO, $n = 5$; mGGO, $n = 17$; and SPN, $n = 9$. There were 21 cases involving the right lung and 10 cases involving the left lung. The mean size of the nodules was 10.3 ±4.1 mm (Table I). All patients’ coagulation functioning was normal prior to surgery.

In the treatment group, 22 subpleural pulmonary nodules (22/23) were successfully located (95.6% accuracy), and an average positioning time of 22.0 ±5.9 min was required (Photo 1). The ultrasonic localisation failed in one patient at the 6 mm posterior basal segment of the left lower lung, where the pGGO was 9 mm away from the pleura because of complications caused by emphysema. The nodule was found after the remedial positioning in combination with extended cuneiform pneumonectomy. In the control group, 31 patients were positioned successfully (31/31; 100% accuracy) with an average positioning time of 24.2 ±5.4 min. The difference in positioning success rate and positioning time was not statistically significant ($p = 0.24; p = 0.15$) between the two groups. The total incidence of complications such as pneumothorax, intrapulmonary haemorrhage and unhooking, and SAS anxiety scores in the treatment group were lower than those in the control group, and the difference was statistically significant ($p = 0.002; p < 0.00$) (Table I). For patients in whom complicated unhooking occurred, the pulmonary nodules were found and removed after re-positioning using a remedial positioning method.

**Discussion**

This study confirmed that CT-guided noninvasive labelling combined with intraoperative percutaneous ultrasound can be used for positioning of subpleural pulmonary nodules/ground-glass opacity in uniportal video-assisted thoracoscopy. The success rate and time for positioning of the CT combined ultrasound group were comparable with that of the preoperative CT-guided puncture, while the incidence of complications and anxiety scores were lower than the latter.

| Parameter               | Experimental group (mean ± SD) | Control group (mean ± SD) | P-value |
|-------------------------|--------------------------------|---------------------------|---------|
| Gender:                 |                                |                           |         |
| Male                    | 7                              | 9                         | 0.91    |
| Female                  | 16                             | 22                        |         |
| Age                     | 46.5 ±22.3                     | 50.1 ±18.6                | 0.45    |
| Location of nodules:    |                                |                           |         |
| Right lung              | 17                             | 21                        | 0.62    |
| Left lung               | 6                              | 10                        |         |
| Size of nodule [mm]     | 11.4 ±6.3                      | 10.3 ±4.1                 | 0.24    |
| Type of lesion:         |                                |                           |         |
| pGGO                    | 4                              | 5                         |         |
| mGGO                    | 14                             | 17                        |         |
| SPN                     | 5                              | 9                         |         |

$pGGO$ – pure ground glass opacity, $mGGO$ – mixed ground glass opacity, SPN – solid pulmonary nodule.
The application value of computed tomography in combination with intraoperative noninvasive percutaneous ultrasonic localisation of subpleural pulmonary nodules/ground-glass opacity in uniportal video-assisted thoracoscopy

The popularity of high-resolution CT makes possible early lung cancer diagnosis and treatment and, accordingly, improved prognosis. Thoracoscopic resection is the preferred option for the diagnosis and treatment of pulmonary nodules. Moreover, a uniportal thoracoscope is widely used because it requires a small incision, few cuts, and minor pain. For positioning in the case of subpleural nodules, experienced thoracic surgeons often combine this with CT images, anatomy, and finger palpation. However, in clinical practice, it was found that the smaller the pulmonary nodules, the closer the character to that of lung pa-

Photo 1. A – Preoperative high-resolution CT showed mGGO of the upper left lung, with a size of 10 × 13 mm (red arrow), a shortest distance skin marker was made (blue dot). B – Percutaneous ultrasound was performed near the CT marker to detect the subpleural nodules (10 mm below visceral pleura, green dot) during the operation, and guide the hook wire to the mGGO. C – CT marker (blue dot) and ultrasonic marker (red dot) have small distance between each other and a good repeatability. D – Hook wire needle was observed under uniportal thoracoscopy, and a pulmonary wedge resection was performed at least 2 cm away from the puncture point. E – Postoperative subpleural nodules were found with naked eye, and pathological indicated infiltrating adenocarcinoma. An extended lobectomy was performed.
renchyma, and the more difficult it was to palpate and locate them. In uniportal thoracoscopic surgery, the surgery area for palpation is additionally limited. If the nodule is far away from the incision or the lung is poorly collapsed, and even when a hypo-solid or solid nodule is below the pleura, it can be difficult to palpate using fingers, whereas the GGO can be almost impossible to locate, even in ex vivo lung tissue [5]. A hybrid operating room and electromagnetic navigational positioning technology [6, 7] present significant technical requirements for doctors, as well as extended surgery times. The equipment involved in these contexts is expensive and often takes a long time to operate in the surgical theatre. As such, it is not conducive to extensive promotion.

At present, imbedding of the hookwire, micro spring coil, and using methylene blue and medical glue are typically employed for preoperative CT positioning [8]. Preoperative puncture positioning is an invasive procedure during which patients must bear complications such as pneumothorax, pleural reaction, and bleeding (lung and chest wall) caused by local anaesthesia puncture, physiological suffering such as pain and limitations to breathing and motion, and psychological burdens such as tension and anxiety [7]. In the present study, the incidence of unhooking and pneumothorax in the control group was significantly higher compared with the treatment group. It was assumed that patients’ breathing, coughing, and thorax movement following the puncture led to the loosening of the puncture needle and secondary lung injury. In the treatment group, the primary nodule localisation (localisation only, no puncture) was affected using only one CT scan. Because no anaesthesia and puncture procedures were completed prior to surgery, no complications occurred. Patients were able to easily cooperate with the procedure and had to endure only a short positioning time, and low scanning dose and cost. The positioning time could be flexibly arranged on the day of the procedure or the day prior to the procedure, without immediate surgery following positioning. Because the puncture was performed after effecting general anaesthesia, there was no pain throughout the entire procedure, even when complications occurred, and no risk of positioning failure caused by unhooking. As a result, the anxiety scores for the positioning procedure were significantly lower compared with the control group. The reduction of overall complications reflected the advantage of this essentially noninvasive approach, which was more acceptable to the patients.

Ultrasound is a method that can accurately estimate the shape, edge, echo, blood flow, acoustic shadow, and compressibility of specific lesions. Research results [9–12] showed that the effect of ultrasound-guided real-time biopsy of lung lesions close to the pleura, or within 10 mm of the pleura, was the same as for CT-guided biopsy. The procedure includes advantages such as good safety and low cost. Japanese scholars [13] found that in the case of lung tissue collapse, an intraluminal ultrasound can find the lung tissue structure within 30 mm of the pleura and can locate the pure GGO at a diameter less than 20 mm. Hironobu [14] selected pig lungs, rabbits, and other animal models as research objects. In the case of atelectasis, a special thoracoscopic ultrasound probe was able to accurately locate the sub-centimetre pulmonary nodules, where the average nodule size was 8.5 ±2.1 mm and the mean depth was 7.4 ±7.5 mm. This evidence indicates that if there is no obvious gas interference on the surface of pulmonary nodules, it is feasible for the subpleural nodules or even the GGO to be located by percu-

| Parameter                  | Experimental group (mean ± SD) | Control group (mean ± SD) | P-value |
|----------------------------|-------------------------------|---------------------------|---------|
| Positioning success rate    | 22/23                         | 31/31                     | 0.24    |
| Positioning time [min]      | 22.0 ±5.9                     | 24.2 ±5.4                 | 0.15    |
| Complications:              | 5                             | 24                        | 0.002   |
| Pneumothorax                | 3                             | 12                        | 0.037   |
| Intrapulmonary haemorrhage  | 2                             | 6                         | 0.27    |
| Unhooking                   | 0                             | 6                         | 0.025   |
| Number of CT scans          | 1                             | 3                         | –       |
| SAS Anxiety Score           | 55.4 ±3.5                     | 64 ±5.2                   | < 0.001 |
The application value of computed tomography in combination with intraoperative noninvasive percutaneous ultrasonic localisation of subpleural pulmonary nodules/ground-glass opacity in uniportal video-assisted thoracoscopic surgery

Chongqing Science and Health Joint Medical Research Project 2021. General program.
Fund Number: 2021MSXM214.
Project Name: The application of computed tomography combined with ultrasound for noninvasive localisation of peripheral pulmonary nodules in single-port thoracoscopic surgery.

Conflict of interest
The authors declare no conflict of interest.

References
1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA Cancer J Clin 2016; 66: 7-30.
2. Weinstock T, Kidambi P, Channick CL, et al. Implementation of lung cancer screening programs with low-dose computed tomography in clinical practice. Ann Am Thorac Soc 2016; 13: 425-7.
3. Wahidi MM, Goevert JA, Goudar RK, et al.; American College of Chest Physicians. Evidence for the treatment of patients with pulmonary nodules: when is it lung cancer? ACCP evidence-based clinical practice guidelines (2nd edition). Chest 2007; 132 (3 Suppl): 94S-107S.
4. Seo JM, Lee HY, Kim HK, et al. Factors determining successful computed tomography-guided localization of lung nodules. J Thorac Cardiovasc Surg 2012; 143: 809-14.
5. Mattioli S, D’Ovidio F, Daddi N, et al. Transthoracic endosonography for the intraoperative localization of lung nodules. Ann Thorac Surg 2005; 79: 443-9.
6. Lempel JK, Raymond DP. Intraoperative percutaneous microcoil localization of small peripheral pulmonary nodules using cone-beam CT in a hybrid operating room. AJR Am J Roentgenol 2019; 213: 778-81.
7. Zhao ZR, Lau RWH, Yu PSY, et al. Devising the guidelines: the techniques of pulmonary nodule localization in uniportal video-assisted thoracic surgery-hybrid operating room in the future. J Thorac Dis 2019; 11 (Suppl 16): S2073-8.
8. Wang WH, Yu T. Research progress on common localization methods of pulmonary nodules in thoracoscopic surgery. J Modern Onco 2019; 27: 4111-5.
9. Jiang S, Tang Q, Tang JX, et al. Diagnostic of ultrasound-guided and CT guided biopsy for peripheral pulmonary nodules. J Clin Path 2008; 38: 324-8.
10. Beckh S, Bölcskei PL, Lessnau KD. Real-time chest ultrasonography: a comprehensive review for the pulmonologist. Chest 2002; 122: 1759-73.
11. Eberhardt R, Ernst A, Herth FJ. Ultrasound-guided transbronchial biopsy of solitary pulmonary nodules less than 20 mm. Eur Respir J 2009; 34: 1284-7.
12. Zhou WW, Duan YY, Cao TS. Application of two-dimensional ultrasound and color doppler in lung tumors. Chinese J Ultrasound Med 1997; 8: 35-7.
13. Konido R, Yoshida K, Hamanaka K, et al. Intraoperative ultrasonographic localization of pulmonary ground-glass opacities. J Thorac Cardiovasc Surg 2009; 138: 837-42.
14. Wada H, Anayama T, Hirohashi K, et al. Thoracoscopic ultrasonography for localization of subcentimetre lung nodules. Eur J Cardiothorac Surg 2016; 49: 690-7.

15. Miyoshi R, Yamashina A, Nishikawa S, et al. Skin marking with computed tomography at functional residual capacity to predict lung nodule site. Interact Cardiovasc Thorac Surg 2020; 30: 36-8.

Received: 2.07.2020, accepted: 11.10.2020.