The Infusion Of Hemocoagulase Into The Biopsy Tract After A Computed Tomography Percutaneous Transthoracic Lung Biopsy Significantly Reduces Complications.

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Abstract :
Aim : The reduction of pneumothorax and pulmonary haemorrhage during computed tomography (CT)-guided percutaneous transthoracic lung biopsy by the injection of hemocoagulase into the biopsy tract (PTLB).
Materials and Methodologies : Patients scheduled for PTLB between January 2020 and March 2021 who had undetected pulmonary lesions were included in a retrospective investigation. The hemocoagulase group or the non-hemocoagulase group received the patients. Patients in the hemocoagulase group received an injection of hemocoagulase (0.2-0.5 units) in the biopsy tract as the sheath was withdrawn following CT-guided biopsies with a 17 G coaxial system. Pneumothorax and pulmonary haemorrhage consequences were assessed using postoperative imaging scans. To ascertain their relationships with the problems, factors such as the patient's position, the location of the lesion, and the pathological findings were assessed.
Results : There were 100 patients total, 44 of whom were men, with a mean age of 53. Pneumothorax and pulmonary haemorrhage rates were 15% and 13% overall, respectively. In the hemocoagulase group (8% and 6%, respectively) compared to the non-hemocoagulase group (22% and 20%, respectively; p=0.04 and 0.03, respectively), the incidences of pneumothorax and pulmonary haemorrhage were statistically substantially reduced. The difference in hemoptysis between the hemocoagulase (6%) and non-hemocoagulase (2%) groups was not statistically significant (p=0.23). Additionally, there were no statistically significant correlations between the positions, locations of the lesions, or pathological outcomes of the patients and pneumothorax or pulmonary haemorrhage.
Conclusion: After PTLB, the rates of postoperative pneumothorax and pulmonary haemorrhage were decreased by injection of biopsy tract hemocoagulase.

Keywords : Lung biopsy, Hemocoagulase, Pneumothorax, Pulmonary hemorrhage

Introduction

An increasing number of individuals are being identified as having lung nodules thanks to advancements in medical technology and the widespread use of low-dose computed tomography (CT) lung imaging, which necessitates lung biopsy for a pathology diagnosis. 1 A minimally invasive procedure called percutaneous transthoracic lung biopsy (PTLB) can be used to collect lung samples for pathological analysis. Studies have shown that it may diagnose indeterminate intrathoracic lesions with satisfactory sensitivity and specificity2,3,4,5; nonetheless, PTLB has certain drawbacks. The most frequent complication of PTLB is pneumothorax, which affects 20% of patients after the surgery. One to fifteen percent of these individuals get a thoracostomy.6 2-15 % of these individuals get a thoracostomy. 6 With an average frequency of 18%, pulmonary haemorrhage is the second most frequent consequence after PTLB. 7,8 These post-procedure problems can considerably lengthen hospital stays and raise healthcare costs. Pneumothorax and pulmonary haemorrhage following PTLB have either been reduced or prevented using a variety of therapeutic methods. Injecting a sealant into the biopsy tract is one of the options. Fibrin, isobutyl-2-cyanoacrylate, autologous blood clots, regular saline, hydrogel plugs, and other proprietary materials are examples of frequently used sealants. 9, 10, 11, 12 Numerous investigations have looked into the effectiveness, dangers, prices, and accessibility of these sealants. 13, 14, 15.

Materials and Methodologies

Study design and participant selection

Retrospective research was done on patients who underwent PTLB at Luhansk General Hospital in Ukraine between January 2020 and March 2021 and had unidentified pulmonary lesions. The hospital's institutional review board gave the study its approval, and individual consent was not required for this retrospective analysis. Patients who got PTLB had undiscovered pulmonary lesions identified by CT who were chosen based on a study of their medical records. Patients were disqualified if they underwent more than one transpleural passage, experienced a pneumothorax or pulmonary haemorrhage prior to the removal of the biopsy needle, had an unsuccessful first puncture, or had undergone previous chest surgery.

Study Protocol

According to the procedure for the Intelligent Current Regulation Technology Intervention, each patient got a preoperative imaging examination using a 128-section multidetector CT scanner (uCT 760, United Imaging Healthcare). The pulmonary lesion's location and imaging features were recorded. According to whether they got PTLB with or without the use of a hemocoagulase injection to seal the biopsy tract, the patients were divided into two groups: the hemocoagulase and non-hemocoagulase groups. Prior to surgery, routine blood tests were done to make sure that the partial thromboplastin time was 1.5 times the normal range, the international normalized ratio was 1.5, and the platelet count was $\geq$ 50,000 cells/μl, Anticoagulant-treated patients were told to stop taking warfarin for $\geq$ 5 days and clopidogrel for $\geq$ 7 days. Depending on the kind of heparin and the need for an anticoagulant, heparin was discontinued for 6–24 hours. Before the biopsy, aspirin continued to be taken. 8,19 Two skilled interventional radiologists with experience in performing percutaneous lung biopsies carried out all of the biopsy operations. Both groups underwent the same PTLB procedures.

The patients relaxed, breathed regularly, and stayed motionless throughout the PTLB when they were in the supine, prone, or lateral decubitus positions. The radiologists chose the best entry route based on the location of the pulmonary lesion in the preoperative CT scans to reduce the length of the biopsy tract and prevent puncturing through pleural fissures, emphysematous areas, bullae, blebs, large blood vessels, and obstructions, like the scapula or ribs. A skin marker and laser lights were utilised to designate the skin after the lesions were located in the uCT 760 CT scanner. For local anaesthesia, a 23 G needle was used to sterilely inject 2–5 ml of 1% lidocaine into the pleura at the location of the skin puncture. Under CT guidance, a 17 G guiding needle (coaxial introducer needle, Argon Medical Devices, TX, USA; MCXS1815BP) was introduced to access the lesion's superficial surface. The biopsy was finished with the help of an 18 G automated cutting needle (BioPince Full Core Biopsy Instrument, Argon Medical Devices; 360-1580-01). For each patient, one to four biopsy samples were collected. The coaxial sheath was removed from the hemocoagulase group while 0.2 to 0.5 units of hemocoagulase (3-5 ml of 0.1 kU/ml) were gently injected into the biopsy tract at the location of the skin puncture. The coaxial sheath was removed from the non-hemocoagulase group without the injection of hemocoagulant.

To rule out pneumothorax and pulmonary haemorrhage, a low-dose CT thorax scan was performed before the patients were allowed to leave the operating room. 20 All patients were then sent to the recovery area. The patients didn't laugh, talk, stretch, or cough much while they were supine for 4 hours. Two radiologists with a combined experience of more than > 10 years examined every CT image and radiograph. If the pneumothorax was less than < 5%, patients just got supportive treatment. Patients who had clinical symptoms and a pneumothorax of between 5 - 20 % had air aspirated through the coaxial sheath (with a 17 G guiding needle). The usual approach was used to place a 6 F chest tube in patients with mild pneumothorax (20–40%). An insert of a 6 F chest tube with a watertight seal was given to patients with a significant pneumothorax ($\geq$ 40%). 21 When there were fresh consolidations or ground-glass opacities in the immediately postoperative CT pictures, pulmonary haemorrhage was taken into consideration. The previously described approach was used to grade the pulmonary haemorrhage severity. 7 There was no evidence of pulmonary haemorrhage, grade 0. Grade 1 showed 2 cm or less of bleeding along the needle tract. Grade $\geq$ 2 refers to sub-lobar haemorrhage that is wider than > 2 cm. Grade 3 denoted larger or lobar bleeding. Haemothorax and hemodynamic instability were indicated by grade 4. Supportive care was provided to patients with Grade 1 haemorrhage, however appropriate clinical measures were needed for Grade 2 or higher haemorrhage.

Outcomes Evaluation

The key outcomes were the number of problems, such as pneumothorax, pulmonary haemorrhage, and hemoptysis, identified in postoperative pictures or reported by patients, as well as the number of pneumothorax and pulmonary haemorrhage requiring clinical interventions. Pneumothorax and pulmonary haemorrhage risk variables made up the secondary outcome assessments. Age, gender, medication history, and a history of chronic lung illness or bleeding were all patient-related factors. Lesion location, size (mean of the maximum and short length of the target lesion), and histological diagnosis were all parameters associated to the lesion (malignancy disease, benign disease, infection lesion, and non-diagnostic lesion). Procedure duration (the amount of time from the guiding needle's insertion to withdrawal), needle adjustment times, puncture pleural times, pleura-needle angle (the acute angle between a line perpendicular to the pleura and the needle trajectory), lung biopsy tract length, and needle adjustment times were all technology-related factors (length in the lung parenchyma traversed by the needle from the pleura to the targeted lesion).

Statistical Analysis

In SPSS, statistical analysis was done (version 25, SPSS, Chicago, IL, USA). For categorical variables, the chi-square test or Fisher's exact tests were used for inter-group comparisons, and the Student's t-test was used for continuous variables. Statistical significance was defined as a p-value > 0.05.

Results

Baseline characteristics of study participants

The investigation comprised 100 individuals with undetermined pulmonary lesions who received PTLB. There were 56 ladies and 44 males, ranging in age from 22 to 85. (mean 53 years). 50 patients were split equally between the hemocoagulase and non-hemocoagulase groups. In neither group was there any mortality noted. Fig. 1 depicts the patient selection procedure. In terms of lesion-related parameters, biopsy method, and demographic characteristics, there were no significant differences between the two groups (Table 1). Figures 2 and 3 provide case studies of pulmonary haemorrhage and PTLB with and without hemocoagulase infusion.

Table 1: Comparisons of baseline characteristics between groups.

Characteristics	Hemocoagulase group (n=50)	Non-hemocoagulase group (n=50)	p-Value a

Age, year, mean ± SD	60 ± 12	64 ± 11	0.12
Lesion size, cm, mean ± SD	2.7 ± 1.5	2.8 ± 1.8	0.85
Biopsy tract distance, cm, mean ± SD	2.5 ± 1.5	2.3 ± 0.9	0.59
CT attenuation of biopsy tract, HU, mean ± SD	801 ± 54	779 ± 91	0.89
Needle size, 17/18 G coaxial, n (%)	50 (100)	50 (100)	1.00
Lesion location, n (%)			0.59
Upper lobe	21 (42)	23 (46)	
Middle lobe	25 (50)	21 (42)	
Lower lobe	4 (8)	6 (12)	
Number of specimens, mean (SD)	3.4 ± 0.9	3.3 ± 0.8	0.66
Operate position, n (%)			0.63
Supine	29 (58)	28 (56)	
Prone	4 (8)	2 (4)	
Other	17 (34)	20 (40	
Pleura–needle angle, degree, mean ± SD	63 ± 23	69 ± 16	0.15
Operation time, minutes, mean ± SD	16 ± 7	17 ± 5	0.71
Times of adjusted needles, mean ± SD	4.4 ± 2.2	4.4 ± 1.4	0.96
Pathology reports, n (%)			0.74
Malignancy	34 (68)	35 (70)	
Benign	12 (24)	13 (26)	
Infection	3 (6)	2 (4)	
Non-diagnostic lesion	1 (2)	0 (0)	

Fig 1 : Patient selection.

SD, standard deviation.

a Chi-square test for categorical variables and Student's t-test for continuous variables.

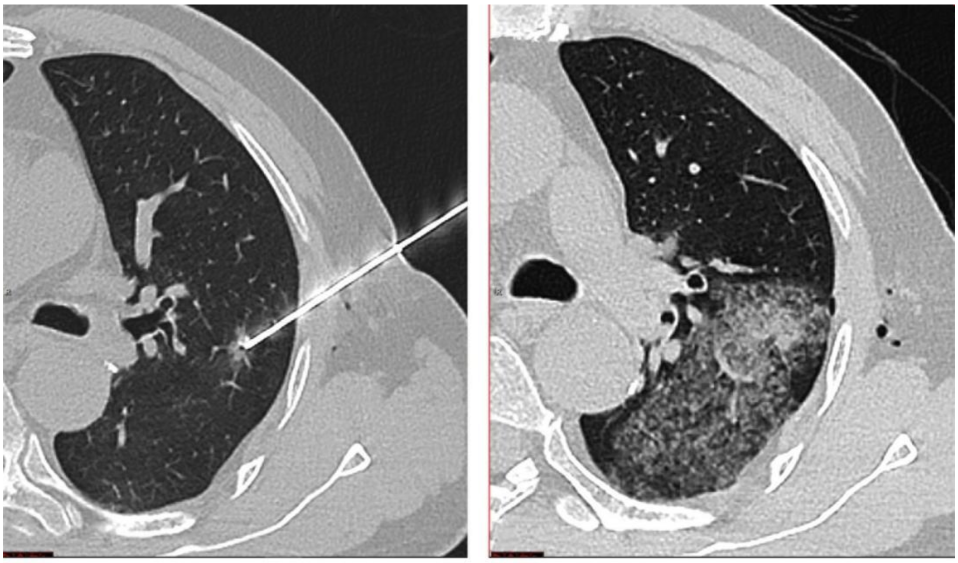

Figure 2 : (a) A 54-year-old man with a 1.8 cm nodule in the left upper lobe. During PTLB, he was placed in the supine position. The lesion was approached from the anterior chest wall. An axial unenhanced CT image (lung window) acquired during the procedure shows the 17 G coaxial needle positioned adjacent to the lesion.

(b) CT image immediately after the biopsy was performed with an 18 G automated cutting needle without hemocoagulase injection to seal the tract. CT image shows Grade 2 haemorrhage, with new ground-glass and consolidative opacity along the needle tract, measuring >2 cm in width. The nodule was confirmed to be adenocarcinoma by a histopathological examination.

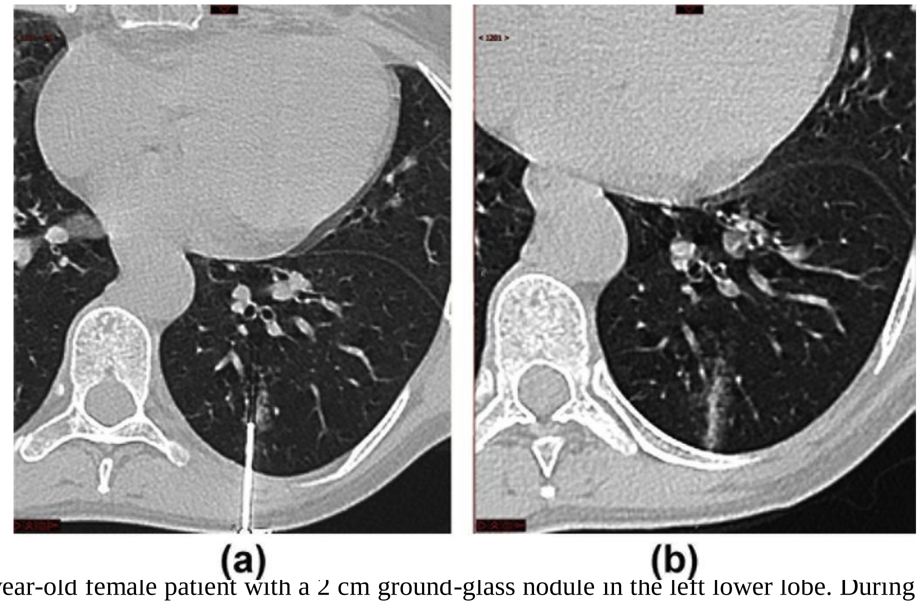

Figure 3 : (a) A 63-year-old female patient with a 2 cm ground-glass nodule in the left lower lobe. During PTLB, she was placed in the prone position. The lesion was approached from the posterior chest wall. An axial unenhanced CT image (lung window) acquired during the biopsy shows the 17 G coaxial needle positioned adjacent to the lesion in the left lower lobe.
(b) CT image immediately after the biopsy with hemocoagulase injected to seal the tract. The CT image shows no pulmonary haemorrhage and the biopsy tract is filled with hemocoagulase. The pathological examination revealed adenocarcinoma.

Postoperative complications are analyzed between two groups.

15% of people had pneumothoraxes total. In the hemocoagulase and non-hemocoagulase groups, the occurrences were 8% and 22%, respectively, with a statistically significant difference (p=0.04; Table 2). One patient in the non-hemocoagulase group also required the insertion of a chest tube and drainage.

Table 2 : Comparisons of postoperative complications between groups.

Complications	Hemocoagulase group (*n*=50)	Non-hemocoagulase group (*n*=50)	*p*-Value
Pneumothorax, *n* (%)	4 (8)	11 (22)	0.04a
<5%	3 (6)	7 (14)	
5–20%	1 (2)	3 (6)	
20–40%	0	1 (2)	
>40%	0	0	
Pulmonary haemorrhage, *n* (%)	3 (6)	10 (20.0)	0.03a
Grade 0	47 (94)	40 (80)	
Grade 1	3 (6)	7 (14)	
Grade 2	0	2 (4)	
Grade 3	0	1 (2)	
Grade 4	0	0	
Hemoptysis, *n* (%)	3 (6)	2 (4)	0.23b

a Chi-square test , b Fisher's exact test.

13 patients, or 13%, suffered from pulmonary haemorrhage. The occurrences were 6% and 20%, respectively, with a statistically significant difference between the hemocoagulase and non-hemocoagulase groups (p=0.03; Table 2). All pulmonary haemorrhage episodes were mild and didn't need any additional treatment. Five individuals (5%) in all reported hemoptysis. Between the hemocoagulase group (6% hemoptysis) and the non-hemocoagulase group (2% hemoptysis; p=0.23), there was no statistically significant difference in hemoptysis.

Postoperative Consequences and Patient Characteristics

The position of the patient (Table 3), the location of the lesion (Table 4), and the pathological outcomes were not statistically significantly linked with pneumothorax and pulmonary haemorrhage sequelae (Table 5).

Table 3 : Comparison of complications between different positions.

Complications	No. Of lung biopsies				*p*-Value a
	All (*n*=100)	Supine (*n*=44)	Prone (*n*=46)	Other (*n*=10)	
Pneumothorax, *n* (%)	15 (15)	6 (13.6)	7 (15.2)	2 (20)	0.63
Pulmonary haemorrhage, *n* (%)	13 (13)	8 (18.1)	4 (8.7)	1 (10)	0.53

a Fisher's exact test.

Table 4 : Comparison of complications between upper, middle, and lower lobes.

Complications	No. Of lung biopsies				*p*-Value a
	All (*n*=100)	Upper (*n*=48)	Middle (*n*=6)	Lower (*n*=31)	
Pneumothorax, *n* (%)	15 (15)	9 (15.8)	0 (0)	6 (16.2)	0.12
Pulmonary haemorrhage, *n* (%)	13 (13)	8 (14)	2 (33.3)	3 (8.1)	0.49

a Fisher's exact test.

Table 5 : Comparison of complications between different types of pulmonary lesions.

Complications	No. Of lung biopsies					*p*-Value a
	All (*n*=100)	Malignancy (*n*=69)	Benign (*n*=25)	Infection (*n*=5)	Non-diagnostic (*n*=1)	
Pneumothorax, *n* (%)	15 (15)	8 (11.6)	6 (24)	1 (20)	0 (0)	0.48
Pulmonary haemorrhage, *n* (%)	13 (13)	9 (13)	3 (12)	1 (20)	1 (100)	0.94

a Fisher's exact test.

Discussion

A popular minimally invasive method for obtaining lung samples for pathological diagnosis is CT-guided PTLB. Additionally, it has a good diagnostic yield and is safe. 23 Pneumothorax and pulmonary haemorrhage, the two most typical side effects of PTLB, can greatly lengthen hospital stays and raise medical costs. Pneumothorax can turn into tension pneumothorax, a potentially fatal illness that needs to be identified and treated very away. Massive Haemothorax and severe hemoptysis are two more consequences that necessitate prompt treatment. 24 Reduced incidence and severity of these postoperative problems are thus crucial. Numerous methods have been documented to slow or stop the growth of these problems. 25,26. Changing the patient's position before, during, and after the biopsy is an example of a postoperative intervention designed to prevent problems. Retrospective research involving patients who had lung biopsies that were guided by CT was described by Appel et al. They discovered that patients in positions with the lesion below the trachea had a low incidence of pneumothorax but not pulmonary haemorrhage or hemoptysis.25,26 This finding was consistent with another study that found a low incidence of pneumothorax when patients were placed in the puncture-side down position as opposed to a supine or prone position.27 However, Leger et al. did not notice a decrease in the pneumothorax. Additionally, a postoperative patient may find it difficult to keep the puncture-side down posture for an extended amount of time or because it is painful. More research is needed to determine the puncture-side down position's possible advantages.

The use of sealants in the biopsy tract to avoid problems following surgery has been researched. 29 McCartney et al. published the initial report on this technique in 1974. 30 The effectiveness of autologous blood coagulation in lowering the occurrence of postoperative pneumothorax was investigated by the researchers. Since then, numerous substances, including Gelfoam pulp, hydrogel plug, regular saline, and fibrin glue, have been tried to seal the biopsy tract. After lung biopsy, Khorochkov et al. successfully reduced the severity but not the incidence of postoperative pneumothorax by injecting saline into the biopsy tube. 31. Li et al. demonstrated that saline injection decreased the incidence of postoperative pneumothorax as well as the requirement for chest tube insertion. 32 Ahrar et al. discovered that self-expanding sealing devices greatly reduced the incidence of postoperative pneumothorax and the need for chest tubes in a randomised experiment employing a hydrogel plug. Studies in series 10 that looked at embolic and tract sealants showed positive impacts on pneumothorax rates. 33 The results of the current study showed that patients who had PTLB could successfully minimize postoperative pneumothorax by injecting hemocoagulase into the biopsy tract. Few earlier research investigated pulmonary haemorrhage; the majority only addressed postoperative pneumothorax. Pulmonary haemorrhage has been shown to be influenced by a variety of circumstances. 34 The current study demonstrated that patients who underwent PTLB could successfully minimize postoperative pulmonary haemorrhage by receiving injections of biopsy tract hemocoagulase. The incidence of pulmonary haemorrhage in the non-hemocoagulase group was 20%, which was comparable to earlier data. 7,8 This incidence was considerably reduced to 6% in the hemocoagulase group. There was no discernible difference in the incidence of hemoptysis between the two groups. The short sample size and low incidence rates of hemoptysis in both groups may be to responsible for this.

When it comes to coagulation, hemocoagulase functions similarly to thrombin and thromboplastin. Des-A-fibrin, a monomer made by blood thrombin-like enzymes, can unite with natural fibrinogen to form a complex that allows it to stay in solution. At the site of arterial lesions, these large molecular weight complexes can increase platelet aggregation and decrease capillary permeability. Hemocoagulase can start coagulation complexes after topical administration into the lung biopsy tract. It can restrict airflow into the pleural cavity and block visceral and parietal pleura puncture sites, which lowers the likelihood of pneumothorax. Blood coagulation can be aided by hemocoagulase, which can also lessen bleeding inside the biopsy tract. Blood clot formation can also speed up the closure of the biopsy tract, lowering the risk of pulmonary haemorrhage and postoperative pneumothorax. The single-center strategy, retrospective design, and brief postoperative follow-up time are among the study's drawbacks. Subgroup analyses to compare individuals with various degrees of pneumothorax or pulmonary haemorrhage were not done because of the small sample size. The testing of pulmonary function, which may have an impact on surgical recovery, was also not done. To verify the current findings, additional prospective studies with sizable sample sizes should be conducted.
In conclusion, the current study demonstrated that patients having PTLB had a lower incidence of postoperative pneumothorax and pulmonary haemorrhage when hemocoagulase was administered in the biopsy tract.

Conflict of Interest

The authors declare no conflict of interest.

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