Diagnostic yield and complications of transthoracic computed tomography-guided biopsies

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ABSTRACT

INTRODUCTION: The widespread use of computed tomography (CT) improves detection of pulmonary lesions, which are not only detected at an increased rate but also at a smaller size. CT-guided lung biopsies are now more frequently used than fluoroscopy-guided lung biopsies. The main aim of the present paper was to investigate the outcome and complications of the biopsies.

METHODS: We retrospectively collected the results and information from 520 CT-guided thorax biopsies. All biopsies were performed with CT-guided "beam-through" technique, using a 64-slice CT scanner.

RESULTS: In 86% of the biopsies, the tissue material was found to be sufficient. In 32% of the biopsies, a complication arose, mostly pneumothorax (30%), but chest drainage was needed in only 15% of the 520 cases. Patients with more than ten cigarette pack-years had a complication risk that was twice as high at that of patients with fewer pack-years. We found that the risk of pneumothorax increased the further the lesion was from the skin surface, the smaller the lesions were and when the patient was biopsied in a lateral position. We also found a higher risk of complications in females than in males.

CONCLUSIONS: CT-guided biopsy is an excellent tool for analysing pulmonary lesions. The present study clearly shows that the risk of developing a pneumothorax is significantly increased among smokers and former smokers with more than ten pack-years.

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Lung cancer is the second most common cancer measured by the number of new annual cases in men and women. The widespread use of CT improves detection of pulmonary lesions which are detected at an increased rate but also at smaller sizes. Radiologists are therefore now attempting to biopsy smaller lesions than in the past. Because of this trend, we probably need to accept a certain decline in diagnostic success and an increase in complication rates because it is occasionally difficult to hit these sometimes very small lesions.

CT-guided lung biopsies are now more frequently used than fluoroscopy guidance [1]. All thorax biopsies carry a certain risk of complications; most commonly pneumothorax and haemoptysis. Although other studies have analysed risk factors in CT-guided lung biopsies [2-4], no Danish reports on identification of procedure-related risk factors or complications exist. The present study is a retrospective analysis of CT-guided thorax biopsies performed at our department with a view to determining which risk factors associated with needle biopsies. The main purpose of the present article is to investigate the outcome of the biopsies with respect to diagnostic accuracy, histological and cytological diagnoses and complications.

METHODS

The study was approved by the Danish Data Protection Agency

We retrospectively collected results and information about 520 CT-guided thorax biopsies performed at our hospital from January to December 2012. Data were collected from the Radiology Information System (RIS), the Picture Archiving and Communication System (PACS), the Electronic Patient Journal (EPJ) and from WEB Pathology (an electronic reporting system for pathological findings).

A total of 562 biopsies had been scheduled. Among those, 42 were excluded because the patient's diagnosis was already clear, blood parameters were outside the safe levels for undergoing a biopsy, or because patients did not show up at the hospital on the day of the biopsy. The study included 427 patients (235 males and 192 females) whose mean age was 67.8 years (range: 22-92 years). They all underwent a total of 520 biopsies.

A total of 334 patients (78%) had one biopsy performed, 79 patients (19%) underwent the biopsy procedure twice, and 14 patients (3%) had three biopsies performed.

The majority of biopsies (478) were performed by an experienced radiologist (more than 50 CT-guided biopsies prior to the study), and 42 of the biopsies were done by radiology residents who were supervised by an experienced radiologist.

All biopsies were performed with CT-guided "beam-through" technique, using a 64-slice CT scanner (Phillips Brilliance 64, Eindhoven, Netherlands). We aimed at a biopsy angle as close to 90 degrees with respect to the pleura as possible.

We used non-coaxial technique. The core needle bi-

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opsies were performed with an 18-gauge core needle (Angiotech, Stenløse, Denmark) (**Figure 1**). The tissue samples were placed on sterile millipore paper and sent for histological examination in a formalin suspension. The fine-needle aspirations were performed with a 0.8 × 80 mm sterile needle (Sterican, Braun, Melsungen, Germany) and the tissue material was placed on objective glass and sent for cytological examination.

Prior to the biopsies, all patients had a blood sample taken from which haemoglobin (Hgb) and coagulation parameters were evaluated. The biopsy levels were set at Hgb concentration > 5 mmol/l, coagulation factor normal test (coagulation factor II, VII, X) > 0.4, activated partial thromboplastin time < 40 sec. and thrombocytes > 40 × 10^9/l. A lung function test was also performed and the biopsy level was set at a forced expiratory volume in the first sec. ≥ 1 l. The patients arrived at the hospitals' Department of Pulmonary Medicine on the day of the biopsy. They were then escorted to the CT room at the Department of Radiology. After the biopsy, the patients returned to the Department of Pulmonary Medicine. The patients were observed for two hours and then an X-ray of the chest was performed. Patients without pneumothorax were dismissed from the hospital.

Patients with pneumothorax were either observed overnight or, if treatment was needed, treated with drainage. Parenchymal bleeding seen on CT was not registered as a complication in the present study since none of the patients showed symptoms correlating with this feature. Patients with more than one complication were all registered with the most treatment-claiming complication.

Patients with either haemoptysis or vasovagal symptoms together with a pneumothorax were registered as a pneumothorax complication. Patients with haemoptysis and vasovagal symptoms were registered as haemoptysis. One patient who died due to the procedure and was registered as such, suffered from both pneumothorax and haemoptysis, and developed a cardiac arrest following the procedure.

The lesion size and the distance from the skin or pleura to the lesion were measured from the CT on the day of the biopsy.

The calculation of pack-years used in the analysis was defined as daily number of cigarettes smoked, multiplied by years of smoking divided by 20.

Statistics

Descriptive statistics were used, and $p < 0.05$ was considered statistically significant. Data were analysed with the Number Cruncher Statistical Systems (NCSS 8 statistical software, Kaysville, UT, USA).

Trial registration: not relevant.

RESULTS

Out of 444 successfully performed biopsies, the material was found to be malignant in 241 cases. Adenocarcinomas and squamous cell carcinomas were the most common malignant diagnoses (**Table 1**).

The patient was a never-smoker in only 16 cases; and in 92 of the cases, the patient was a former smoker, the remaining patients were current smokers.

No small cell carcinomas or squamous cell carcinomas were found in biopsies from never-smokers or smokers with less than ten pack-years.

Out of the 520 biopsies, six cases were excluded as they had not been registered in the Web Pathology Register. In 444 (86%) out of 514 biopsies, the tissue material was found to be sufficient (**Table 2**). As shown in Table 2, only the lesion size had a statistically significant influence on the successful completion of the biopsy.

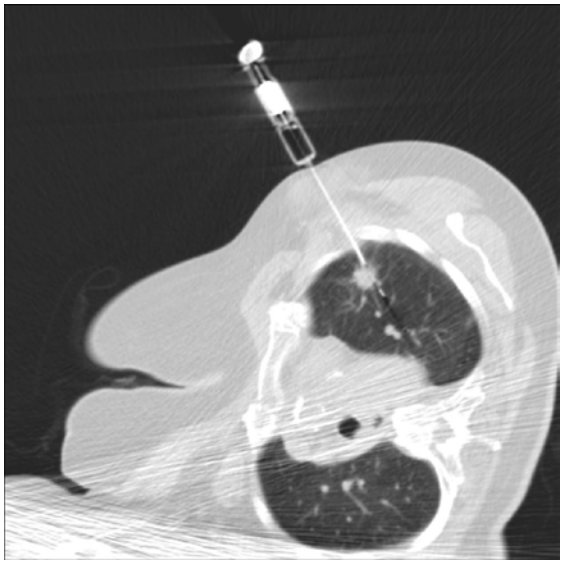
Complications were encountered in 33% (167 out of 520) of the biopsies; 154 of these patients were diagnosed with a pneumothorax. In 15% (79 out of 520) of the biopsies, chest drainage was needed. A 73-year-old male with disseminated lung cancer and poor lung and cardiac function died immediately after the thorax biopsy procedure.

Biopsies of patients with more than ten cigarette pack-years had a complication rate twice as high as biopsies of patients with fewer pack-years (**Table 3**).

The complication rate and the need for treatment were clearly higher among smokers and former smokers

FIGURE 1

Computed tomography-guided core needle biopsy performed from a lesion in the left lung, with the patient in lateral position.



than among never-smokers. Only 13% of the never-smokers developed a pneumothorax compared with approximately 30% in the group of smokers and former smokers. Every fourth patient among the never-smokers required chest drainage, while this was the case in approximately every second patient in the group of smokers or former smokers. We found an increased risk of developing a pneumothorax when the patient was biopsied in a lateral position, $p < 0.001$ (Table 3), (Figure 1). This may be due to the increased lung movement that occurs in this position. In a prone position, there is less lung movement. We found a significantly increased risk for developing a pneumothorax when the biopsy was obtaied 5-10 cm from the skin surface as compared with when it was obtained less than 5 cm from the skin surface (Table 3). There was also a higher risk of developing a pneumothorax when the lesions were less than 1 cm in diameter (Table 3). We found that every fourth male and every third female developed a pneumothorax. Haemoptysis was also more common in females than in males (Table 3).

We performed a total of 93 re-biopsies or second re-biopsies. We did not find a higher incidence of complications in these biopsies than in the remaining biopsies.

DISCUSSION

This study shows a correlation between certain risk factors and complications. We demonstrate that the complication rate and the need for treatment are higher among smokers and former smokers with more than ten pack-years than among never-smokers. The risk of developing pneumothorax is also increased when the lesions are smaller or the biopsy route is long. We found an increased risk of pneumothorax when patients were biopsied in a lateral position. This is in line with the findings reported in other studies [5-7]. We did not observe an increased risk of complications in patients with reduced lung function; but like Branden et al [5], we found an increased risk of treatment-dependent complications in patients with reduced lung function. This was also reported by Yeow et al [4]. In the 520 biopsies reported in the present study, one was fatal due to cardiac arrest in a male multimorbid patient. This yields a mortality rate of 0.2% in the present study of CT-guided biopsies, which is in line with the rates reported in other studies [5]. Considering that patients who undergo lung biopsies are typically not otherwise healthy, the risk of serious complications may be considered quite low. Other studies have reported similar results [5, 8].

The diagnostic yield depended on the lesion size as an improved yield was associated with increased lesion size (Table 2). This result is in line with those reported in other studies [3, 9, 10]. We found no small cell carcinomas or squamous cell carcinomas in the group of never-smokers or in the group of smokers with fewer than ten pack-years. Hence, these histological findings seem to be induced primarily by heavy smoking, which is in accordance with the observation made by Pesch et al [11].

TABLE 1

Pathological diagnoses from 444 successfully performed computed tomography-guided biopsies.

Diagnosis	n
Adenocarcinoma	126
Small cell carcinoma	21
Squamous cell carcinoma	46
Metastases	21
Other malignant diagnoses	27
Non-malignant diagnoses	203

TABLE 2

Diagnostic yield in computed tomography-guided biopsies. The values are n.

Characteristic	Successful biopsy	Failed biopsy	p-value
Lesion size, cm			0.000001
< 1	9	6	
1-4	276	54	
> 4	159	10	
Lesion localisation			0.5
Upper lobe	227	39	
Lower lobe	188	26	
Middle lobe	15	4	
Thorax wall	14	1	
Patient positioning			0.9
Prone	247	40	
Supine	111	18	
Lateral position	86	12	
Lesion density			0.2
Semisolid	138	28	
Cavitating	50	3	
Solid	247	38	
Ground glass opacity	9	1	
Distance from skin surface to lesion, cm			0.3
≤ 2.5	12	1	
2.6-5	166	21	
5.1-10	250	43	
10.1-15	16	5	
Distance from parietal pleura to lesion, cm			0.3
0	181	24	
0.1-1.9	131	16	
2-3.9	98	19	
4-5.9	26	11	
6-18	8	0	

The planning of the biopsy path is very important in minimising the complication rate and also to reduce the necessary exposure time [12]. The planning includes finding the shortest distance to the lesion, avoiding vessels and airways, and avoiding to cross the interlobar spaces. This approach will contribute to keep low the occurrence of complications like pneumothorax and haemorrhage, and it will minimise the rate of seeding. Earlier studies, however, have not shown any increase in pleural carcinomatosis when transthoracic biopsies are compared with transbronchial biopsies [13, 14]. Flechsig found only one out of 146 cases with possible seeding in the thorax wall after biopsy. Although it is seldom, seeding must be avoided whenever possible. This is why it is essential to avoid biopsies across interlobar spaces.

An earlier study has reported only a non-significant difference between complications recorded when using coaxial and non-coaxial techniques, respectively [6]. The authors found complicating pneumothorax in 36.6% of the biopsies that were done with the coaxial technique and 32.3% in biopsies done using the non-coaxial technique. In our study, we used only the non-coaxial technique, and our complication rate was equal to that reported in the Nour-Eldin study. However, in cases in which the nodule is very small, the first specimen can be insufficient for pathological examination; an extra biopsy may therefore be needed. In these cases, the use of a coaxial needle could be an advantage. The main limitation of the present study is that it is not a prospective study, which makes it dependent on information already available in the databases. This left us with some unanswered questions, for instance concerning smoking habits, co-morbidity and lung function. Furthermore, we did not register the pathological findings in patients who underwent a lung resection although the primary biopsies did not show malignant findings. Nonetheless, we were able to get most of the information concerning the actual biopsy procedure because we had access to all the CTs. The strength of this study is the inclusion of a very large number of patients.

For the patients, the period after the biopsy can be associated with a degree of pain [15], which is usually well-tolerated. However, we did not monitor pain in this retrospective study, nor did we monitor the exact level of radiation that the radiologist received during the biopsy. We did, nevertheless, occasionally measure the radiologist's exact hand dose in the last part of the study and introduced sterile radiation-reducing gloves to protect the fingertips, which are at risk of being exposed to the highly collimated CT beams. A study [16] has shown that the median hand dose in CT-guided interventions was 0.22 mSv and the study concluded that the upper limit for the annual hand dose will normally first be reached at approximately 2,000 annual interventions.

In the future, the need for biopsies with histological specimens will increase, although a recent systematic review has shown a similar, high sensitivity and specificity of core needle biopsies and fine-needle aspiration in distinguishing benign from malignant pulmonary lesions [17]. Furthermore, distinguishing between the histological subtypes of the malignant lesions. Owing to the fact that chemotherapeutic treatment is getting more and more specific. This aims for core needle biopsies rather than fine needle aspirations, shown by Choi et al [9] and also recognised in other studies [10, 18]. When

TABLE 3

Risk and complication factors in computed tomography-guided biopsies. The values are n.

	Complications			No	
Characteristic	**pneumothorax**	**haemoptysis**	**other**	**complications**	**p-value**
Gender					0.02
Male	71	2	1	207	
Female	83	10	0	146	
Age, yrs					NS
20-49	9	1	0	9	
50-59	23	2	0	62	
60-69	49	3	0	134	
70-79	52	5	1	108	
80-92	21	1	0	40	
Cigaret pack-years[a]					0.02
< 10	12	4	0	61	
≥ 10	128	6	1	260	
Lung disease					NS
Yes	39	1	1	64	
No	115	11	0	289	
Patient positioning					0.0007
Prone	74	6	1	209	
Supine	35	3	0	92	
Lateral position	45	3	0	52	
Lesion localisation					0.00001
Upper lobe	97	10	0	162	
Lower lobe	46	2	1	168	
Middle lobe	11	0	0	8	
Thorax wall	0	0	0	15	
Thorax half					NS
Right	92	3	1	176	
Left	62	9	0	177	
Distance from skin surface to lesion, cm					0.00001
≤ 2.5	0	0	0	13	
2.6-5	38	3	0	146	
5.1-10	108	6	1	183	
10.1-15	8	3	0	11	
Distance from parietal pleura to lesion, cm					0.00001
0	23	2	0	180	
0.1-1.9	54	3	1	92	
2.0-3.9	51	5	0	62	
4.0-5.9	23	2	0	13	
6.0-18.0	3	0	0	6	
Lesion size, cm					0.00001
< 1	8	0	0	7	
1-5	130	12	1	236	
> 5	16	0	0	110	

NS = non-significant.

a) In 48 cases out of the 520 biopsies there were no information about pack-years.

performing biopsy of ground glass opacities, even core needle biopsies are in many cases insufficient in those cases where determination of the specific cell type of the tumour is essential for treatment planning. In their study from 2013 [19], Yamagami et al showed that the correct specific cell type was revealed in only 55% of the biopsies compared with an operative sampling.

CONCLUSIONS

CT-guided thorax biopsy is a safe diagnostic procedure for obtaining histological and cytological material before treatment and carries only a low risk of serious complications. The risk of complications can be estimated from patient smoking habits, lesion size, location of the lesion, biopsy depth, positioning of the patient and gender.

This study clearly shows that the risk of developing a pneumothorax is significantly higher among smokers and former smokers with more than ten pack-years than among never-smokers. The risk of pneumothorax rises the further the lesion is located from the skin surface and the smaller the lesion is.

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