

Diagnostic Accuracy of CT Readings of Coin Lesions in the Lung as Compared with Transthoracic CT-Guided Needle Biopsy Results

Diagnostische Genauigkeit der CT bei intrapulmonalen Rundherden im Vergleich zu den histopathologischen Resultaten der CT-gesteuerten Biopsie

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Abstract

Background: The aim of this study was to compare chest CT film reading results with histopathological results after CT-guided transthoracic needle biopsy of the lung. In addition, lung lesion morphology was evaluated and compared with the nature of the lesions.

Patients and Methods: Pulmonary lesions of 133 patients who underwent chest CT were retrospectively grouped into benign, malignant or uncertain. All patients underwent CT-guided transthoracic biopsy. Results of CT diagnosis and histopathological evaluation were compared. In addition, CT features such as size, borders, shape and presence of necrosis were assessed and compared with histopathological results.

Results: In 129 patients adequate specimens were obtained. Comparison of CT diagnosis with the histopathological results yielded the following results for chest CT: sensitivity 95%, specificity 43%, positive predictive value 83%, and negative predictive value 75%. Lesions with spiculated margins turned out to be associated with a significantly higher number of malignant lesions than lesions with smooth or blurred margins ($p < 0.05$). Lesions size, lesion shape as well as the presence of necrosis showed no significant relation to nature of the lesions ($p > 0.05$).

Conclusion: Radiological assessment of pulmonary lesions alone is not sufficient. the specificity of chest CT is not sufficient to make a definitive diagnosis, i.e., histological verification is still needed for further investigation in a large number of cases. Only lesions with spiculated margins showed a significantly higher number of malignant degenerations in histological evaluation.

Zusammenfassung

Hintergrund: Zum Vergleich CT-morphologischer Befunde fokaler Lungenherde mit histopathologischen Resultaten der CT-gesteuerten Biopsie. Zusätzlich erfolgte die Auswertung bildmorphologischer Kriterien und deren Vergleich mit der histopathologischen Dignität der Läsionen.

Patienten und Methoden: Computertomografisch detektierte Lungenherde von 133 Patienten wurden retrospektiv in benigne, maligne und unklare Läsionen eingeteilt. Alle Läsionen wurden CT-gesteuert punktiert. Die Ergebnisse der CT-morphologischen Bildanalyse sowie der histopathologischen Evaluation wurden verglichen. Zusätzlich wurden bildmorphologische Kriterien wie Größe, Berandung, Form und das Vorliegen von Nekrosen erfasst und mit den histopathologischen Resultaten verglichen.

Ergebnisse: 129 Patienten wurden erfolgreich punktiert. Der Vergleich der computertomografischen Diagnose mit den histopathologischen Resultaten ergab für die CT eine Sensitivität von 95%, eine Spezifität von 43%, einen positiven Vorhersagewert von 83% sowie einen negativen Vorhersagewert von 75%. Läsionen mit spikulierter Berandung waren signifikant häufiger maligne als Läsionen mit glatter oder unscharfer Berandung ($p < 0.05$). Größe, Form oder vorhandene Nekrosen hatten keinen statistisch signifikanten Bezug zur Läsionsdignität ($p > 0.05$).

Schlussfolgerung: Die Spezifität der CT des Thorax ist zumeist nicht ausreichend für eine endgültige Diagnosestellung, sodass eine histologische Sicherung in der Mehrzahl der Fälle anzustreben ist. Einzig Läsionen mit spikulierter Berandung zeigten in der histopathologischen Evaluation einen signifikant höheren Anteil maligner Befunde.

Introduction

Detection of a pulmonary mass on chest X-ray is routinely followed by chest computed tomography (CT) for further investigation. CT provides better information such as exact localization, size, shape, borders and contrast enhancement, involvement of adjacent structures, lymph node involvement and in cases of malignant disease the detection of metastasis. In association with the imaging criteria mentioned above, CT helps to narrow the diagnostic spectrum. Based on its results, decisions for further invasive investigations are undertaken to confirm the imaging diagnosis histologically. CT-guided percutaneous transthoracic needle biopsy of the lung is a well established method in the histological diagnosis of pulmonary lesions [1–4] and is regarded as a safe procedure with limited morbidity and very rare mortality [1–9]. Pneumothorax and perifocal hemorrhage remain the most frequent complications [5, 6, 8, 10].

Other serious complications such as empyema and seeding of malignant cells into the needle track are rare and should not influence the indications for CT-guided transthoracic needle biopsy [11].

The diagnostic accuracy of this method has been reported and ranges from 64% to 97% [5, 9, 12–20]. So far histological CT-guided biopsy results were only compared to results of postsurgical histological examinations or with long-term CT follow-ups. None of the current studies has compared the chest CT imaging diagnosis with the histological results of transthoracic CT-guided biopsy.

The purpose of the present study was to compare our results of chest CT imaging diagnosis with the histological results of transthoracic CT-guided biopsy with regard to specificity, sensitivity, positive and negative predictive values. In addition the morphology of lesions was assessed and correlated with their histopathology.

Material and Methods

Patients

84 men and 49 women aged 30–83 years (mean age 63.4 years) were included in the study. The pulmonary coin lesions were detected as incidental findings during a chest CT which was primarily conducted for other clinical indications. 91% of the patients were referred to our institution by the various departments of our hospital, 9% of the patients were referred to us by external physicians. Informed consent was obtained from all patients at least 24 hours before biopsy.

CT scanning and interpretation

In all patients, chest CT scans were obtained prior to biopsy. CT scans were obtained by using a 16-row MDCT (multidetector computed tomography; Sensation 16, Siemens Medical Systems, Forchheim, Germany). Scanning was performed in caudo-cranial direction using the helical technique, with 1.5 mm collimation. The exposure parameters for CT scanning were 120 kV and 120 mAs. Each patient received 100 mL of a non-ionic contrast medium at a flow rate of 3.0 mL/sec (Ultravist® 370 mg/mL; Schering Inc., Berlin, Germany) infused through an 18-gauge intravenous antecubital catheter. All scans were analyzed at a lung window (width 2000/center – 500), soft tissue window (width 450/center 50) and bone window (width 2700/center 700). All scans were reconstructed in 5 mm slice thickness and 2.5 mm overlap.

Two staff radiologists, who had more than 10 years of experience in chest CT reading, classified all lesions into benign, malignant or uncertain according to the parameters listed below.

Presence of tumour necrosis: Tumour necrosis was described if the evaluated lesion showed a hypodense center after administration of i. v. contrast medium.

Size: Lesion size was determined along the maximum expansion in two planes in a lung window setting using an electric calliper. Lesions >30 mm in diameter were classified as malignant whereas lesions <10 mm were classified as benign [21]. Lesion size between 11–29 mm was classified as uncertain.

Shape: The shape of the lesion was classified into round, oval, wedge-shaped and polycyclic. Lesions with concave shaped margins were classified as scar tissue whereas lesions with convex shaped margins were classified as proliferative tissue and therefore suspicious for malignancy [21].

Borders: The borders of the lesion was classified into smooth (benign), blurred (uncertain) and spiculated (malignant).

Presence of calcifications: Pulmonary nodules or masses in which fat or calcification without significant contrast medium enhancement were detected were classified as benign hamarthomas or granulomas [21].

Attenuation values before and after contrast media application: Attenuation values before and after contrast medium injection were measured in a solid part of the lesion. Lesions enhancing less than 15 HU were classified as benign, enhancement >25 HU as malignant and enhancement between 16 and 25 HU uncertain [21–23].

Decisions in regard to the features and further treatment were made in consensus if the evaluated lesion had varying numbers of benign and malignant features.

Biopsy procedure

All biopsies were performed under CT guidance by staff radiologists, both of whom had more than 10 years experience in CT-guided transthoracic needle biopsy.

Patients were handled in an outpatient setting whenever possible. 135 percutaneous transthoracic needle biopsies were performed in the 133 patients at our hospital. 2 patients underwent biopsy twice, due to insufficient specimen on the first biopsy. Exclusion criteria were lung lesions smaller than 5 mm in maximum diameter, patients who were not able to follow verbal or visual instructions and patients who refused to give their informed consent. Emphysema was not an exclusion criterion for biopsy.

Before biopsy, coagulation parameters of all patients were checked. It was assured that patients were not taking anticoagulants or aspirin and had normal platelet counts, prothrombin time and activated prothrombin time. Blood sampling was done no longer than 3 days before biopsy. Depending on the location of the lesion procedures were performed with the patient in a prone, supine, or lateral position. No precautions were taken to prevent pneumothorax in terms of patient positioning. Patients were instructed to breathe calmly during the procedure and abstain from talking. Axial images were acquired from the chest before biopsy. Biopsy was monitored by obtaining selected images at the area of interest with 10-mm transverse CT sections. The skin around the puncture site was disinfected with 10% iodine solution and the area was covered sterilely. 10 mL of 1% xylocain were administered subcutaneously as local anesthesia. After skin incision all biopsies were performed with an 18-gauge cutting needle system (Biopsy-Handy®, Somatex® Medical Technologies

Ltd., Teltow, Germany). The cutting needle was manually pushed into the lung lesion and a 20-mm long tissue core was retrieved. If possible fissures, pleural effusions and pleural bullae were avoided during biopsy. Before sampling, the aspiration needle position within the lesion was documented by obtaining axial CT images.

Specimens obtained were immediately immersed in 10% formalin solution and sent for examination to the staff pathologist of our hospital.

Immediately after biopsy a chest CT scan was done to detect pneumothorax or intrapulmonary hemorrhage. After the procedure patients were placed on a stretcher or bed for 4 hours, with the supervision of a nurse. Four hours after the biopsy chest radiographs were obtained with the patient in an erect position for detection of pneumothorax or hemorrhage. Pneumothorax was treated in symptomatic cases or when the pneumothorax was enlarging as compared to the CT obtained just after biopsy.

Statistical analysis

Diagnostic accuracy, i.e., true-positive rate, true-negative rate, false-positive rate, false-negative rate, negative predictive value, positive predictive value, sensitivity and specificity were determined.

True positive was defined as a case in which the CT diagnosis of malignant disease was confirmed histologically. *True negative* was defined as a case in which the initial CT diagnosis of benign disease was confirmed histologically. *False positive* was defined as a case in which a lesion was classified as not benign in chest CT, i.e., malignant or uncertain, but turned out to be benign in histological work-up. *False negative* was defined as a case that was classified as benign in chest CT but turned out to be malignant or uncertain in histological work-up.

Statistical analysis was carried out using the BiAS for Windows software package (Version 8.2, 1989–2006, Epsilon Publishers). The χ^2 test was used to analyze the relationship between size, shape, presence of necrosis, borders of the lesions and their histological nature. Differences were considered significant when the *p* value was below 0.05.

Results

Radiological diagnosis using chest CT classified 93 lesions as malignant, 20 lesions as primarily benign and 22 lesions as uncertain. Histological work-up yielded 94 malignant lesions and 35 benign lesions. 6 cases remained uncertain.

From 93 cases diagnosed as malignant on chest CT 15 cases turned out to be benign and 2 were uncertain after histological work-up. From 20 cases diagnosed as benign on chest CT, 5 cases turned out to be malignant. Only 4 out of the 22 cases remained uncertain after histological evaluation. Two cases could not be classified in histological work-up but have been classified as malignant in chest CT (Table 1).

Out of the 6 cases that remained uncertain after histological evaluation, an insufficient biopsy specimen was sampled in one case, in four cases unrepresentative biopsy specimens were sampled and in another case the suspicious lesion was missed.

95 cases were true positive, 20 cases were false positive, 15 cases were true-negative and 5 cases false negative. The true-positive rate (sensitivity) was 95%, the false-positive rate was 57%, the true-negative rate (specificity) was 43% and the false-negative

Table 1 Comparison of chest CT diagnosis with histopathological evaluation.

	All	Malignant	Benign	Uncertain
Chest CT	135	93	20	22
	Malignant	76 (82%)	5 (25%)	13 (59%)
Histology	Benign	15 (16%)	15 (75%)	5 (23%)
	Uncertain	2 (2%)	0	4 (18%)

Table 2 Lesion margination and its histopathologic distribution.

Borders	n	Malignant	Benign	Uncertain
Smooth	68	44	18	6
Blurred	32	18	14	0
Spiculated	35	32	3	0
	135	94	35	6

Table 3 Lesion size and its histopathological distribution.

Size [cm]	n	Malignant	Benign	Uncertain
≤1	8	6	0	2
>1–2	33	22	9	2
>2–3	29	21	7	1
>3–4	18	17	1	0
>4–6	29	15	14	0
>6–10	14	11	2	1
>10	4	2	2	0
	135	94	35	6

Table 4 Lesion shape and its histopathological distribution.

Shape	n	Malignant	Benign	Uncertain
Round	54	38	10	6
Geometric	19	11	8	0
Oval	31	21	10	0
Wedge-shaped	14	10	4	0
Polycyclic	17	14	3	0
	135	94	35	6

rate was 5%. The positive predictive value was 83% and the negative predictive value was 75% (Table 1).

Lesions with spiculated boundaries turned out to be associated with a significantly higher number of malignant lesions than those with smooth or blurred margins ($p < 0.05$) with a sensitivity of 100% and a positive predictive value of 91%, respectively (Table 2).

Lesion size, lesion shape as well as the presence of necrosis showed no significant relation to nature of the lesions ($p > 0.05$) (Table 3, Table 4).

Complications

Three patients required chest tube placement for treatment of pneumothorax. Intrapulmonary hemorrhage requiring further clinical follow-up occurred in 9 patients. Pneumothorax as well as intrapulmonary hemorrhage resolved within a few days without further invasive interventions, either by chest surgery or by interventional radiology.

Discussion



Because of the high incidence of malignant disease of the chest, and in particular of the lung, every lesion needs to be considered as suspicious until proven otherwise. Therefore biopsy procedures play a major role in the diagnostic cascade in pulmonary disease. This is particularly important when considering the high number of false-positive lesions reported on the largest screening trial NLST (National Lung Screening Trial, 96.4%) [24]. In the last 3 decades several studies have proved the accuracy and safety of image-guided transthoracic lung biopsy procedures [1–9,25].

Reports about diagnostic accuracy have compared histological CT-guided biopsy results with the results of histological examinations after surgery or with long-term CT follow-ups, i.e., these studies reported efficacies which range from 82% to 95% [5, 12, 16–18].

To the best of our knowledge none of these reports compared chest CT imaging diagnosis with the histological results of transthoracic CT-guided biopsy and, as such we have to discuss our results in the context of studies which used histological examinations after surgery or long-term CT follow-ups as a reference.

In this study we found a sensitivity (95%) and a positive predictive value (83%) similar to those reported by previous studies while specificities and negative predictive values were lower [5, 12, 16–18].

Specificities of up to 100% as reported by some authors cannot be confirmed by our data [5, 12, 16–18].

The high rate of false-positive cases in our study results in a specificity of 43% in chest CT diagnosis. This underlines how important the histological work-up of pulmonary lesions is and clearly shows the limitations of chest CT as sole diagnostic method. Even PET/CT turned out to be not specific enough to abandon tissue confirmation [26]. Data about the value of PET/MRI must still be collected and have not been evaluated as yet.

Potential diagnostic features such as lesion shape, lesion size or the presence of necrosis did not show any relation to the nature of the lesion. Although increasing lesion size was reported [21] to be more likely to be malignant, we cannot confirm this from our data. On the other hand, our data clearly confirm reports by several authors [21,27–30] that lesions with spiculated margins are significantly more likely to be linked to malignancy. **Table 1** shows that chest CT diagnosis remains uncertain in more than 16% of the cases, i.e., radiological assessment of pulmonary lesions alone is not sufficient. Even though we found high positive predictive value, negative predictive value and specificity, the overall significance is too low to solely rely on chest CT. In the group of uncertain CT diagnosis, 59% turned out to be malignant after histological evaluation. These results justify that uncertain cases in chest CT are managed as suspicious lesions until proven otherwise. Histological verification helps to reduce the number of uncertain cases significantly ($p < 0.05$) and therefore is still needed for further investigation in a substantial number of cases. Patients benefit from a lower rate of follow-up examinations and a reduction of the associated irradiation. Data from the NSLT [24] and NELSON [31] trials indicate that there is a 20% or even more lung cancer mortality reduction when using low-dose CT as a screening method in selected patients. Other much smaller studies show no stage shift or reduction in mortality [32]. Although these results are currently controversially discussed [33] they have led to changes in recommendations already [34], thus if they are confirmed they may facilitate the use of CT, but at the

same time increase the number of false-positive results leading to further diagnostic investigations.

However, we found a 5% rate of missed (false-negative) diagnoses for malignant lung tissue, i.e., gross naked eye inspection of the sampled tissue core by the radiologist is not a guarantee for successful biopsy [35]. In cases in which there are discrepancies between CT features, clinical presentation and biopsy results, the biopsy should be repeated.

A limitation of this study was that, due to the retrospective nature of data collection, we had no control over the sample size. In this study we focused on a comparison of chest CT imaging diagnosis with the histological results of transthoracic CT-guided biopsy, therefore data from histological work-up of the surgical specimen or long-term CT follow-up studies were not included in this paper.

Our results confirm clinical practice: The combination of both chest CT imaging and further invasive investigations, such as transthoracic CT-guided biopsy, fiber-optic bronchoscopy or open surgery, are useful measures in patients with pulmonary lesions.

Conflict of interest



The authors have no conflict of interest.

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