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Diagnostic value of preoperative chest computed tomography examination in clinical tumor-node-metastasis staging of non-small cell lung cancer

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► ***Original article***

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ABSTRACT

Background: This research aimed to investigate diagnostic value of preoperative chest computed tomography (CT) in the staging of clinical tumor-node-metastasis (TNM) in non-small cell lung cancer (NSCLC). ***Materials and Methods:*** Hundred and ninety eight patients with NSCLC accepted by the Affiliated Hospital of Shaoxing University (Shaoxing Municipal Hospital) from June 2021 to October 2022 were retrospectively selected as the study subjects. Preoperative multislice spiral computed tomography (MSCT) examination was performed, and the results of pathological examination were the gold standard to evaluate accuracy of CT diagnosis of TNM staging. ***Results:*** The staging accuracy of CT diagnosis was 86% for T1, 85.34% for T2, 76.92% for T3, and 66.7% for T4, with an overall accuracy of 83.83%. The Kappa value was 0.744. For nodal staging, the accuracy of CT diagnosis was 85.34% for stage N0, 67.86% for stage N1, and 72.22% for stage N2, yielding an overall accuracy of 79.29%. The Kappa value for nodal staging was 0.702. In terms of specific stages, the accuracy of CT diagnosis was 80.39% for stage IA, 81.40% for IB, 59.38% for IIA, 76.47% for IIB, and 73.21% for IIIA, with an overall accuracy of 75.25%. The Kappa value for these stages was 0.701. ***Conclusion:*** The clinical T stage, N stage, and TNM stage diagnosed by CT before surgery were consistent with the pathological T stage after surgery, especially in the early stage of LC.

INTRODUCTION

In 2020, China reported over 810,000 new cases of lung cancer (LC), constituting about 37% of the global total. The mortality exceeded 710,000, reflecting a high death rate of 87% [1, 2], underscoring the significant threat to human health. LC is categorized into non-small cell lung cancer (NSCLC) and SCLC, with NSCLC accounting for roughly 85% of cases, substantially more than small-cell lung cancer [3]. NSCLC typically exhibits slower cell growth and metastasis, and often lacks distinct symptoms in its early stages [4]. Consequently, patients are frequently diagnosed only when the disease has progressed to advanced stages, limiting treatment options and worsening the prognosis [5-6].

As a standard for cancer staging, the TNM staging system for NSCLC is crucial in determining treatment pathways and prognosis assessment. This system comprises three fundamental components: T (size of the primary tumor and its invasion into surrounding tissues), N (regional lymph node involvement), and M (distant metastasis) [7-9]. Through these detailed classifications, the TNM staging not only illustrates the current state of tumor development but also provides medical teams with a basis for formulating personalized treatment strategies. In practice, TNM staging helps identify early-stage patients suitable for surgical treatment. For patients with middle and late stages, staging information guides doctors in adopting comprehensive treatment plans, including chemotherapy, radiotherapy, targeted therapy, or immunotherapy, aiming to maximize disease control, prolong survival, and improve quality of life [10-12]. With the advancement of medical research, the TNM staging system continuously evolves, more accurately reflecting prognostic differences among various patient groups. Updates may include redefinitions of tumor size, refinements in lymph node involvement classification, and improvements in distant metastasis assessment, ensuring that the staging system aligns with modern treatment methods and patient outcomes. Moreover, TNM staging facilitates international communication and collaboration, enhancing the comparability of clinical trial results and contributing to the global accumulation and advancement of lung cancer treatment [13]. Despite its high utility and universality, the TNM staging system is not without flaws; its accuracy is constrained by the sensitivity and specificity of diagnostic technologies, as well as the consistency in clinical application and understanding of the staging criteria

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among clinicians. Therefore, ongoing research and education are essential for maintaining and improving the accuracy and clinical value of staging.

For the assessment of TNM staging, pathological biopsy results are considered the clinical standard. However, this method is primarily used to confirm the condition post-surgery and is not applicable during the operation. Studies have demonstrated that imaging examinations can be employed for tumor diagnosis, localization, characterization, and staging [14, 15]. MSCT images can effectively reveal the location, size, shape, number, and margins of lung cancer lesions, as well as their relationships with surrounding tissues and the size and distribution of lymph nodes in the hilum and mediastinum [16]. While CT images offer a comprehensive diagnosis of lung cancer, they do not provide sufficient evidence for evaluating TNM staging prior to surgery.

The novelty of this work lies in systematically evaluating practical value of preoperative chest CT examination for clinical TNM staging, particularly in assessing the accuracy of early-stage lung cancer staging. Using a retrospective study design, the research provides a detailed analysis of CT's diagnostic performance in T and N staging, as well as overall TNM staging, and offers robust evidence by directly comparing these findings with postoperative pathological staging.

MATERIALS AND METHODS

Research objectives

A retrospective study was conducted on 198 patients with NSCLC accepted by the Affiliated Hospital of Shaoxing University (Shaoxing Municipal Hospital) from June 2021 to October 2022. Inclusion criteria were: (1) definitive diagnosis by surgical pathology examination; (2) complete pathological examination results and clear pathological stages post-operation; (3) preoperative plain and enhanced chest CT examinations conducted within seven days pre-surgery; (4) complete CT image data; and (5) no prior therapies, including radiotherapy or chemotherapy, before the operation. Exclusion criteria included: (1) preoperative TNM stages N3 or M1, indicating stage IIIB or stage IV lung cancer with distant metastasis without surgical indications; (2) presence of other malignant tumors; and (3) diagnosis of SCLC by pathological examination.

According to the collected statistics, male patients was 110 cases, and female patients was 88 cases. All patients were aged from 30 to 80 years old (average age: 62.83±10.22 years old). On clinical physical examination, all 198 patients had symptoms such as cough and expectoration, among which 167 patients had blood in sputum, 66 patients had chest tightness and shortness of breath, and 52 patients had chest and back pain. Regarding tumor location, 62 cases were in right lung, with 45 cases in lower lobe, 12 cases in middle lobe, 47 cases in upper lobe of left lung, and 32 cases in lower lobe of left lung. All patients underwent TNM staging, with two professional radiologists independently evaluating and staging the imaging results. In cases of disagreement, a third radiologist made the final decision. The impact of CT examination on TNM staging was assessed based on the pathological staging results. All patients included in the study received notification, consent, and approval from the relevant medical ethics committee.

CT examination methodologies

In this study, all patients were examined using 64-row 128-slice spiral CT (SOMATOM Definition AS German). The scan range extended from the thoracic inlet to the adrenal glands. All patients fasted for six hours prior to the examination, and respiratory guidance was provided to help patients master breathing techniques, facilitating a better scan by the operators. The parameters for the plain scan were as follows: Tube voltage was 120 kV, tube current was 150 mA, layer thickness was 2.5 mm, spacing was 2.3 mm, pitch was 1, and matrix was 512 ×512. All patients underwent plain scan followed by enhanced examination of the area of interest. Enhanced scanning was performed with a gold nanoparticle contrast agent at a dose of 100 mL, which was injected intravenously at 2.0~2.5 mL/s.

Image analysis

CT images of all patients were collected, and then two physicians with deputy director titles or higher independently reviewed the images on the Picture Archiving and Communication System (PACS) (LANWON Technology Co., Ltd, China). They guided the CT images to the postprocessing system, which combined plain scan images, enhanced scan images, and thin-layer reconstructed images. This process allowed for a comprehensive analysis of tumor lesions, including their location, size, number, morphology, and extent. In cases of discrepancy between the evaluations, the diagnosis of a higher-level physician was sought, and consultation was conducted to reach a consensus.

TNM staging

In this study, CT and pathological TNM staging were under the eighth edition of the Union for International Cancer Control Lung Cancer TNM staging standard, which was officially promulgated and implemented in 2017. The T stage primarily assesses the primary tumor, including the lesion's location, size, and extent of infiltration, and is denoted as TX or T0-T4. The N stage evaluates regional lymph node metastasis, considering factors such as metastatic station number and the presence of skip metastasis, which can influence patient

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prognosis. This stage is represented as NX or N0-N3. The M stage examines the presence of distant metastasis, including the identification of metastatic organs and the number of metastatic foci, and is classified as MX, M1a, M1b, or M1c. Specific evaluation methodologies are shown in table 1 [17].

Table 1. TNM staging criteria for the eighth edition of NSCLC.

Index			Concrete manifestations
T stage	TX		The size cannot be measured; Tumor cells are present but no lesions are found
	T0		No primary lesion is found
	Tis		Carcinoma in situ
	T1	T1a	Maximum diameter ≤1 cm, lung and visceral pleura; Or located on the wall of the tube, any size
		T1b	2 cm≥ maximum diameter > 1 cm, other things are the same as T1a.
		T1c	3 cm≥ maximum diameter > 2 cm, other things are the same as T1a.
	T2	T2a	4 cm≥ maximum diameter > 3 cm, involving the main bronchus, visceral pleura (less than carina), atelectasis, and pneumonia.
		T2b	5 cm≥ maximum diameter > 4 cm, others are the same as T2a.
	T3		7 cm≥ maximum diameter > 5 cm, involving chest wall, pericardium, and phrenic nerve. Two or more nodules in the same leaf
	T4		The largest diameter is more than 7 cm, involving diaphragm, mediastinum, trachea, esophagus, heart, great vessels, carina, spine, and laryngeal nerve. There are two or more nodules in different lobes of the same lung.
N stage	Nx		Impossible to judge
	N0		No metastasis
	N1		Ipsilateral bronchus/hilum
	N2		Ipsilateral mediastinum and/or subcarina
	N3		Contralateral mediastinum and/or hilum of lung, and/or congruent, contralateral anterior scalene/supraclavicular lymph
M stage	Mx		Impossible to judge/no metastasis
	M0		No distant metastasis
	M1a		Chest mold diffusion
	M1b		Extrathoracic single site
	M1c		Extrathoracic multiple sites

Observation indexes

Preoperative CT images of all patients were collected to obtain T stage, N stage, and M stage results of preoperative CT diagnosis of patients. According to results, the specific staging of LC was obtained, including stage IA (including stages 1–3), stage IB, IIA, IIB, and IIIA (table 2). The difference and consistency of the two diagnostic results were analyzed under pathological diagnosis results.

Statistical methodologies

In this work, *SPSS 22.0* (IBM, USA) was employed. The consistency between clinical and pathological CT staging results was assessed using the Kappa test. The criteria for consistency were as follows: unsatisfactory for Kappa < 0.4, satisfactory for 0.4 ≤ Kappa < 0.75, and highly satisfactory for Kappa ≥ 0.75. P<0.05 suggested that the difference had statistical significance.

Table 2. Clinical stage evaluation criteria (Refer to Table 1 for abbreviations in this table).

	N0	N1	N2	N3
T1a	IA1	IIB	IIIA	IIIB
T1b	IA2			
T1c	IA3			
T2a	IB			
T2b	IIA			
T3	IIB	IIIA	IIIB	IIIC
T4	IIIA			
M1a	IVA			
M1b				
M1c	IVB			

Note: The pink areas are LC stages observed in this study. The remaining stages did not have surgical indications and were not studied.

RESULTS

Staging statistics

Pathological T stages after surgery were T1, T2, T3, and T4. The distribution of patients was 50 cases in T1, 108 cases in T2, 30 cases in T3, and 11 cases in T4. Pathologically diagnosed as T1 in 50 cases, CT diagnosed as T1 in 43 cases, T2 in 7 cases, T3 in 0 cases, T4 in 0 cases. Pathologically diagnosed as T2 in 108 cases, CT diagnosed as T1 in 7 cases, T2 in 99 cases, T3 in 2 cases, T4 in 0 cases. Pathologically diagnosed as T3 in 30 cases, CT diagnosed as T1 in 0 cases, T2 in 6 cases, T3 in 20 cases, T4 in 2 cases. Pathologically diagnosed as T4 in 11 cases, CT diagnosed as T1 in 0 cases, T2 in 2 cases, T3 in 4 cases, T4 in 4 cases. The preoperative CT findings for the T stages were as follows: 50 patients in T1 stage, 116 patients in T2 stage, 26 patients in T3 stage, and 6 patients in T4 stage (table 3). The accuracy of CT staging compared to pathological staging was 86% for T1, 85.34% for T2, 76.92% for T3, and 66.7% for T4. Notably, accuracy decreased with increasing T stage. The overall accuracy of CT diagnosis relative to pathological diagnosis was 83.83%. The Kappa value was 0.744, indicating satisfactory consistency.

Table 3. Statistics of T-staging of preoperative CT diagnosis and postoperative pathological diagnosis (Refer to table 1 for abbreviations in this table).

		Pathological stage (example)					Total	Accuracy
		T1	T2	T3	T3	*P*		
CT staging (example)	T1	43	7	0	0	<0.05	50	86%
	T2	7	99	6	2	<0.05	116	85.34%
	T3	0	2	20	4	<0.05	26	76.92%
	T4	0	0	2	4	<0.05	6	66.67%
Total		50	108	30	11	<0.05	198	83.83%
P		<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

N staging statistics

Statistical results showed that the postoperative pathological N staging of stage N0, stage N1, and stage N2 patients was divided into 116 patients at stage N0, 34 patients at stage N1, and 48 patients at stage N2. Pathologically diagnosed as N0 in 116

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cases, CT diagnosed as N0 in 99 cases, NI in 6 cases, and N2 in 11 cases. Pathologically diagnosed as N1 in 34 cases, CT diagnosed as N0 in 11 cases, NI in 19 cases, and N2 in 4 cases. Pathologically diagnosed as N2 in 48 cases, CT diagnosed as N0 in 6 cases, NI in 3 cases, and N2 in 39 cases. Pathologically diagnosed as N0 in 116 cases, CT diagnosed as N0 in 99 cases, NI in 6 cases, and N2 in 11 cases. Pathologically diagnosed as N1 in 34 cases, CT diagnosed as N0 in 11 cases, NI in 19 cases, and N2 in 4 cases. Pathologically diagnosed as N2 in 48 cases, CT diagnosed as N0 in 6 cases, NI in 3 cases, and N2 in 39 cases. Preoperative CT diagnosis results for stages N0, N1, and N2 were as follows: 116 patients with stage N0, 28 with stage N1, and 54 with stage N2 (table 4). The accuracy of CT staging compared to pathological staging was 85.34% for stage N0, 67.86% for stage N1, and 72.22% for stage N2. The overall accuracy of CT diagnosis relative to pathological diagnosis was 79.29%. The Kappa value was 0.702, indicating satisfactory consistency.

Table 4. Statistics of N-staging of preoperative CT diagnosis and postoperative pathological diagnosis (Refer to table 1 for abbreviations in this table).

		Pathological stage (example)			*P*	Total	Accuracy
		N0	N1	N2			
CT staging (example)	N0	99	11	6	<0.05	116	85.34%
	N1	6	19	3	<0.05	28	67.86%
	N2	11	4	39	<0.05	54	72.22%
Total		116	34	48	<0.05	198	79.29%
P		<0.05	<0.05	<0.05	<0.05	<0.05	

Clinical staging statistics

Clinical staging results of preoperative CT diagnosis and postoperative pathological diagnosis were analyzed. It showed that the distribution of postoperative pathological clinical staging was 50 patients with stage IA, 41 with stage IB, 32 with stage IIA, 19 with stage IIB, 54 with stage IIIA, and 2 with stage IIIB. Pathologically diagnosed as stage IIA in 50 cases, CT diagnosed as stage IIA in 41 cases, stage IB in 2 cases, stage IIA in 7 cases, and stage IIB in 0 cases. Pathologically diagnosed as stage IB in 41 cases, CT diagnosed as stage IIA in 2 cases, IB in 35 cases, IIA in 2 cases, and IIB in 0 cases, IIIA in 2 cases. Pathologically diagnosed as stage IIA in 32 cases, CT diagnosed as stage IIA in 3 cases, IB in 3 cases, IIA in 19 cases, IIB in 0 cases, and IIIA in 7 cases. Pathologically diagnosed as stage IIB in 19 cases, CT diagnosed as stage IIA in 2 cases, IB in 0 cases, IIA in 0 cases, IIB in 13 cases, and IIIA in 4 cases. Pathologically diagnosed as stage IIIA in 54 cases, CT diagnosed as stage IIA in 1 case, IB in 4 cases, IIA in 4 cases, IIB in 4 cases, and IIIA in 41 cases. Pathologically diagnosed as stage IIIB in 2 cases, CT diagnosed as stage IIA in 0 cases, IB in 0 cases, IIA in 0 cases, IIB in 0 cases, and IIIA in 2 cases. Preoperative CT scans were conducted for 50 patients with stage IA disease, 43 patients with stage IB disease, 32 patients with stage IIA disease, 17 patients with stage IIB disease, and 56 patients with stage IIIA disease (Table 5). The accuracy of CT staging compared to pathological staging was 80.39% for stage IA, 81.40% for stage IB, 59.38% for stage IIA, 76.47% for stage IIB, and 73.21% for stage IIIA. The overall accuracy of CT diagnosis relative to pathological diagnosis was 75.25%. The Kappa value was 0.701, indicating satisfactory consistency. Figure 1 shows CT images for different clinical stages.

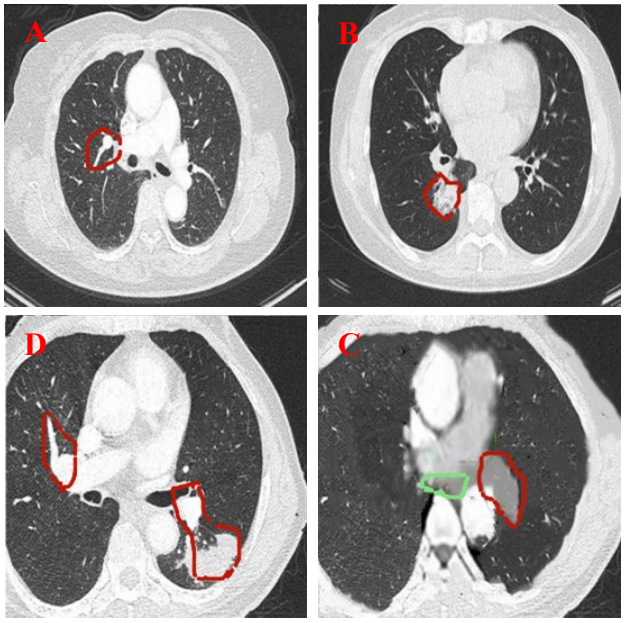


Figure 1. CT images of different clinical stages (**A** is IA, **B** is IB, **C** is IIIA, **D** stands for lymph node metastasis, red indicates primary tumor, and green indicates metastatic lymph nodes).

Table 5. Clinical staging statistics of preoperative CT diagnosis and postoperative pathological diagnosis (Refer to table 1 for abbreviations in this table).

		Pathological stage (example)							Total	Accuracy
		IA	IB	IIA	IIB	IIIA	IIIB	*P*		
CT staging (example)	IA	41	2	3	2	1	0	<0.05	50	80.39%
	IB	2	35	3	0	4	0	<0.05	43	81.40%
	IIA	7	2	19	0	4	0	<0.05	32	59.38%
	IIB	0	0	0	13	4	0	<0.05	17	76.47%
	IIIA	0	2	7	4	41	2	<0.05	56	73.21%
Total		50	41	32	19	54	2	<0.05	198	75.25%
P		<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

DISCUSSION

As the most common malignant tumor in clinical practice, NSCLC cannot be optimally treated by surgery once it progresses to intermediate or advanced stages [18]. Currently, CT imaging technology is a widely used method for evaluating NSCLC, with MSCT offering superior image processing capabilities. This technology can clearly depict tumor morphology, size, and distribution, facilitating the evaluation of disease stages prior to clinical surgery [19]. Numerous clinical studies have demonstrated that accurate TNM staging before surgery is crucial for formulating appropriate therapy plans and assessing NSCLC

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patients' prognosis [20, 21]. Nevertheless, pathological staging remains the standard in clinical practice, requiring the acquisition of pathological tissue through invasive procedures. NSCLC TNM staging system demonstrates significant advantages and inevitable limitations compared to other conventional staging methods. Its strengths lie in providing a comprehensive and detailed staging framework that considers not only tumor size, local lymph node involvement, and distant metastasis, but also closely correlates with patient prognosis, providing a strong basis for personalized treatment strategies and survival prediction. Moreover, as an internationally recognized standard, TNM staging promotes global clinical research and practice exchange. However, the system faces challenges, including its high dependency on advanced imaging and pathological technologies, and potential disparities in technical resources among different medical institutions that may affect staging accuracy. Additionally, TNM staging relies on subjective clinical judgment at certain staging nodes, posing consistency challenges. Furthermore, the system requires continuous learning due to frequent updates, and currently does not fully integrate molecular biomarker information, which is crucial in the era of precision medicine. Nevertheless, TNM staging remains the most comprehensive and widely applied system in current NSCLC staging. Continued efforts in optimization and integrating biomarkers will further enhance its clinical value.

This study compared and analyzed the results of preoperative CT diagnosis and postoperative pathological staging, including T staging, N staging, and TNM staging. Regarding T staging, the overall accuracy of CT and pathological diagnosis was 83.83%, with a Kappa value of 0.744, indicating satisfactory agreement between CT-T staging and pathological T staging. Since T staging assesses tumor size, location, and extent of invasion [22], these results suggest that chest MSCT effectively displays these characteristics with high accuracy. Colombi *et al*. (2022) [23] also confirmed that CT scans can evaluate tumor size and facilitate clinical T staging. However, T1-T4 staging can be influenced by factors such as the presence of atelectasis or pneumonia, the nature of intrapulmonary nodules, and both subjective and objective observer variables [24]. Therefore, improving T staging accuracy necessitates a comprehensive evaluation adhering to established standards. Regarding N staging, the condition of lymph nodes determines whether surgical treatment is feasible for patients with tumor diseases, making the accuracy of N staging crucial for tailoring therapeutic regimens for NSCLC [25]. In this study, the overall accuracy of CT diagnosis compared to pathological diagnosis was 79.29%, with a Kappa value of 0.702, indicating satisfactory consistency in N staging. Similar results were reported by Kucuker *et al*. (2022) [26]. For TNM staging, the total accuracy of CT diagnosis relative to pathological diagnosis was 75.25%, with a Kappa value of 0.701, reflecting satisfactory consistency and diagnostic value for NSCLC TNM staging. In early-stage NSCLC patients, where tumors are small and lymph node metastasis is absent, CT staging results were more aligned with pathological staging [27]. Specifically, the accuracy of CT in diagnosing stage IA (80.39%) and stage IB (81.40%) was higher compared to stage IIA, IIB, and IIIA. Additional studies have demonstrated that imaging examinations generally offer higher staging accuracy for tumor diseases [28, 29]. Therefore, CT plays a valuable role in evaluating LC TNM staging.

CONCLUSION

This study compared the application of preoperative CT with pathological TNM staging in NSCLC, highlighting CT's high accuracy in early-stage lung cancer staging. Despite demonstrating consistency between CT staging and pathological staging, particularly in early stages, the study still has some shortcomings, including its relatively small sample size and retrospective design. Future research should expand sample sizes, extend follow-up periods, and enhance the universality and timeliness of results to advance more precise clinical diagnostic practices.

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***Author contribution*:** X.X. designed the study. J.X. and L.W. conducted the research. B.L. and B.H. provided assistance and advice for the experiments. X.X. and J.X. performed the data analysis. All authors contributed to the editing and revision of the

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manuscript. All authors read and approved the final manuscript. All authors were fully involved in the work and agree to be accountable for all aspects of the research.

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