THE ROLE OF COMPUTED TOMOGRAPHY IN THE DIAGNOSIS OF LUNG ADENOCARCINOMA

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Abstract

Lung adenocarcinoma is the most common histological type of lung cancer, occupying a leading position in oncological morbidity and mortality worldwide. This article provides a detailed analysis of the role, capabilities, modern methods, and clinical significance of computed tomography (CT) in the diagnosis of lung adenocarcinoma. CT examination is the "gold standard" for detecting lung adenocarcinoma at early stages, assessing tumor size, local invasion, lymph nodes, and distant metastases. Modern low-dose CT (LDCT) screening programs have reduced lung cancer mortality by 20-25%. CT semiotics characteristic of adenocarcinoma include: ground-glass opacities (GGO), the "spiculation" sign, the "halo" sign, the vacuole sign, and cavitation. CT-based TNM staging is crucial for determining prognosis and selecting treatment tactics. Recently, artificial intelligence and deep learning models (CNN-LSTM-RF) allow for automatic analysis of CT images, distinguishing adenocarcinoma from other histological types with up to 97% accuracy. The article also covers epidemiological indicators in the Central Asian region, differential diagnosis, and future prospects of CT examination.

Keywords: lung adenocarcinoma, computed tomography, low-dose CT, CT semiotics, TNM staging, artificial intelligence, deep learning, differential diagnosis.

Аннотация

Аденокарцинома лёгкого является наиболее распространённым гистологическим типом рака лёгкого и занимает одно из ведущих мест в структуре онкологической заболеваемости и смертности во всём мире. В данной статье подробно проанализирована роль компьютерной томографии (КТ) в диагностике аденокарциномы лёгкого, её возможности, современные методы и клиническое значение. КТ-исследование считается «золотым стандартом» в выявлении аденокарциномы лёгкого на ранних стадиях, оценке размеров опухоли, локальной инвазии, состояния лимфатических узлов и отдалённых метастазов. Современные программы скрининга с использованием низкодозной КТ (LDCT) позволили снизить смертность от рака лёгкого на 20–25%. К КТ-семиотическим признакам аденокарциномы относятся: очаги по типу «матового стекла» (GGO), симптом «спикул», симптом «гало», вакуольный признак и кавитация. На основе КТ проводится стадирование по системе TNM, что имеет решающее значение для определения прогноза и выбора тактики лечения. В последние годы технологии искусственного интеллекта и модели глубокого обучения (CNN-LSTM-RF) позволяют автоматически анализировать КТ-изображения и дифференцировать аденокарциному от других гистологических типов с точностью до 97%. В статье также освещены эпидемиологические показатели в регионе Центральной Азии, вопросы дифференциальной диагностики и перспективы развития КТ-исследований в будущем.

Ключевые слова: аденокарцинома лёгкого, компьютерная томография, низкодозная КТ, КТ-семиотика, стадирование TNM, искусственный интеллект, глубокое обучение, дифференциальная диагностика.

Annotatsiya

O‘pka adenokarsinomasi o‘pka saratonining eng keng tarqalgan gistologik turi bo‘lib, butun dunyoda onkologik kasallanish va o‘lim ko‘rsatkichlarida yetakchi o‘rinlardan birini egallaydi. Ushbu maqolada o‘pka adenokarsinomasini diagnostikasida kompyuter tomografiyasi (KT) tekshiruvining roli, uning imkoniyatlari, zamonaviy usullari va klinik ahamiyati batafsil tahlil qilingan. KT tekshiruvi o‘pka adenokarsinomasini erta bosqichlarda aniqlash, o‘smaning hajmi, lokal invaziyasi, limfa tugunlari va uzoq metastazlarni baholashda "oltin standart" hisoblanadi. Zamonaviy past dozali KT (LDCT) skrining dasturlari o‘pka saratonidan o‘limni 20-25 foizga kamaytirgan. KT-semiotikada adenokarsinomaga xos belgilar: mayin to‘qimali tugunlar (GGO), "spikula" belgisi, "halo" belgisi, vakuola belgisi va kavitatsiya. KT asosida TNM-stadialash prognozni aniqlash va davolash taktikasini tanlashda hal qiluvchi ahamiyatga ega. So‘nggi yillarda sun’iy intellekt va deep learning modellari (CNN-LSTM-RF) KT tasvirlarini avtomatik tahlil qilib, adenokarsinomani boshqa gistologik turlardan 97 foizgacha aniqlik bilan farqlash imkonini beradi. Maqolada Markaziy Osiyo mintaqasidagi epidemiologik ko‘rsatkichlar, differentsial diagnostika va KT tekshiruvining kelajakdagi istiqbollari ham yoritilgan.

Kalit so‘zlar: o‘pka adenokarsinomasi, kompyuter tomografiyasi, past dozali KT, KT-semiotika, TNM-stadialash, sun’iy intellekt, deep learning, differentsial diagnostika

Introduction

Lung cancer ranks among the leading causes of oncological morbidity and mortality worldwide [1,2]. According to the Global Burden of Disease 2021 data, lung cancer deaths exceeded 2.1 million globally in 2021, accounting for approximately 18% of all cancer deaths [1]. Among all histological types of lung cancer, adenocarcinoma is the most common, comprising 40-50% of all cases [2,3]. In developed countries, this figure can reach up to 60% [4].

In the Central Asian region, including Uzbekistan, lung cancer incidence rates have shown an increasing trend in recent years. According to GBD 2021 data, the standardized incidence of lung cancer in Central Asia is 25-30 per 100,000 population [1]. However, the implementation of modern CT screening programs in the region is insufficient, leading to late-stage detection of the disease [22].

A characteristic feature of adenocarcinoma is its frequent peripheral location in the lung and its asymptomatic course for a long period [5,6]. This leads to diagnosis at late stages, often after the development of metastases. According to statistics, 57% of patients with lung cancer are diagnosed at the stage of distant metastases (M1) [7].

Early detection of lung adenocarcinoma significantly improves survival rates. The 5-year survival rate for stage I lung cancer is 70-80%, whereas for stage IV, it drops below 5% [8,9]. Therefore, developing effective screening and early diagnostic methods is an extremely urgent issue.

Computed tomography (CT) is the primary and most informative method for diagnosing lung adenocarcinoma. While standard radiography has low sensitivity (20-30%) for detecting early-stage lung cancer, CT examination provides 90-95% sensitivity [10,11]. The National Lung Screening Trial (NLST) showed that low-dose CT (LDCT) screening reduces lung cancer mortality by 20% [12]. The NELSON trial reported a reduction of 25% [13].

Lung adenocarcinoma exhibits specific semiotic signs on CT examination. The most characteristic signs include: ground-glass opacity (GGO), the "spiculation" sign (spike-like projections at the nodule margins), the "halo" sign (presence of a ground-glass zone around the nodule), the vacuole sign (presence of gas bubbles within the nodule), and cavitation (necrosis within the nodule) [14,15,16]. The combination of these signs is important for differentiating adenocarcinoma from other histological types [16].

Beyond detecting lung adenocarcinoma, CT examination plays a crucial role in its staging according to the TNM system. Modern multi-slice CT (MSCT) and contrast-enhanced CT methods provide high accuracy in assessing tumor size (T), regional lymph nodes (N), and distant metastases (M) [17,18].

In recent years, the development of artificial intelligence and deep learning technologies has ushered in a new era in CT diagnostics. The CNN-LSTM-RF hybrid model developed by Alashban et al. (2026) can distinguish histological types of lung cancer based on CT images with 97% accuracy [19]. Such

technologies create significant opportunities for reducing radiologists' workload, increasing diagnostic speed, and minimizing subjective errors [46].

The purpose of this article is to comprehensively analyze the role of computed tomography in the diagnosis of lung adenocarcinoma, its modern capabilities, CT semiotic features, and prospects for integration with artificial intelligence technologies.

Main Part

EPIDEMIOLOGY AND CLINICAL SIGNIFICANCE

Lung adenocarcinoma is a malignant tumor located in the peripheral parts of the lung, with a glandular-like structure. It accounts for 40-50% of all lung cancer cases and is more common in women and non-smoking patients [2,3,4].

According to the Global Burden of Disease 2021 study, the number of new lung cancer cases worldwide in 2021 was 2.4 million. Of these, approximately 1.1-1.2 million are attributed to adenocarcinoma [1]. Among women, adenocarcinoma occurs 2-3 times more frequently than other histological types [4].

Significant regional variations are observed. In East Asia (China, Japan, Korea), adenocarcinoma accounts for 60-70% of all lung cancer cases, which is associated with genetic factors and a high frequency of oncogenic mutations [20,21]. In North America and Western Europe, this figure is 40-50% [2,3].

Although complete statistical data on lung adenocarcinoma in the Central Asian region is limited, available studies indicate that the proportion of adenocarcinoma has significantly increased over the past 20 years. From 25-30% in the 1990s, this figure has now reached 40-45% [22].

Risk factors. The main risk factors for developing lung adenocarcinoma include [23,24,25]: Smoking is the primary risk factor, associated with 70-80% of all cases. However, adenocarcinoma is more common in non-smokers compared to other histological types. In non-smokers, adenocarcinoma accounts for 50-60% of all lung cancer cases [24]. Passive smoking increases the risk of developing lung adenocarcinoma in non-smoking women by 20-30% [24].

Genetic factors – oncogenic mutations such as EGFR, KRAS, ALK, ROS1 play a significant role in adenocarcinoma development. In East Asia, EGFR mutations occur in 40-50% of cases, whereas in Europe and North America, this figure is 10-20% [20,21]. Air pollution – high concentrations of PM2.5 particles increase the risk of lung adenocarcinoma by 15-20% [25]. Radon and asbestos are occupational risk factors in the workplace [23].

Clinical course characteristics. Lung adenocarcinoma grows slower than other histological types and remains asymptomatic for a long period [5,6]. Initial symptoms are usually non-specific: prolonged cough, hemoptysis, chest pain, shortness of breath, weight loss. In peripherally located tumors, symptoms may not appear for a long time [5].

An important feature of adenocarcinoma is its tendency for early metastasis. Hematogenous spread to the brain, bones, liver, and adrenal glands can develop even when the primary tumor is small [6,26]. This characteristic further emphasizes the need for early diagnosis and complete staging.

PHYSICAL AND TECHNICAL BASICS OF COMPUTED TOMOGRAPHY AND MODERN METHODS

Several modern variants of CT examination are used in the diagnosis of lung adenocarcinoma [14,17,18].

Low-dose computed tomography (LDCT). Low-dose CT is an examination method performed with a 4-5 times lower radiation dose (1-2 mSv) than standard CT, used primarily for screening purposes [12,13]. The National Lung Screening Trial (NLST) showed that LDCT screening reduces lung cancer mortality by 20% [12]. The NELSON trial reported a reduction of 25% [13].

The main indications for LDCT screening are: age 50-80 years; smoking history of more than 20 years (pack-year index ≥20); current smoker or quit within the last 15 years; absence of symptoms [27].

High-resolution computed tomography (HRCT). High-resolution CT is a CT method performed with thin slices (1-2 mm) and high spatial resolution, allowing detailed visualization of the structural details of the lung parenchyma [14,28]. HRCT is the "gold standard" for assessing the morphological characteristics of pulmonary nodules (shape, margins, internal structure, relationship with surrounding tissue) [28].

Contrast-enhanced computed tomography. Contrast-enhanced CT is performed after intravenous administration of an iodine-based contrast agent and is used to assess blood vessels, tumor vascularity, lymph nodes, and distant metastases [17,18]. Contrast-enhanced CT has high sensitivity for detecting mediastinal lymph nodes (N-staging) and metastases to the liver and adrenal glands (M-staging) [18].

Multi-slice computed tomography (MSCT). Multi-slice CT is a modern CT method with multiple detector rows, allowing acquisition of 64, 128, 256 or more slices per rotation [17]. Advantages of this method include: short examination time (a few seconds); high spatial and temporal resolution; capability for three-dimensional (3D) reconstruction and multiplanar reformatting; ability to examine the entire chest and abdomen simultaneously [17].

CT perfusion and spectral CT. These advanced methods allow assessment of tumor vascularity (perfusion) and tissue composition [29]. CT perfusion is used to assess tumor angiogenesis, while spectral CT is used to determine the iodine concentration in tumor tissue. These methods provide additional information in the differential diagnosis of benign and malignant nodules [29].

CT SEMIOTICS OF LUNG ADENOCARCINOMA

Lung adenocarcinoma exhibits several characteristic semiotic signs on CT examination. Knowledge of these signs is crucial for accurate diagnosis and differential diagnosis [14,15,16].

Ground-Glass Opacity (GGO). Ground-glass opacities appear on CT images of the lung parenchyma as hazy, non-uniform areas that still allow visualization of bronchi and blood vessels [14,15,30]. GGO is one of the most characteristic signs of lung adenocarcinoma, particularly observed in non-invasive (AIS – adenocarcinoma in situ) and minimally invasive (MIA – minimally invasive adenocarcinoma) forms [30]. CT types of GGO include [14,30]: pure GGO – the nodule consists entirely of a ground-glass component; part-solid GGO (mixed GGO) – a solid component in the center of the nodule with a peripheral GGO zone; solid nodule – the nodule consists entirely of a solid component. Malignant features of GGO include [15,30]: increase in size over time; appearance or increase of the solid component; indistinct, irregular margins; presence of the "spiculation" sign.

Spiculation sign – the presence of spike-like, radially oriented projections at the nodule margins, is a characteristic feature of lung adenocarcinoma [16,31]. This sign reflects invasive growth of the tumor tissue into the surrounding lung parenchyma. The sensitivity of the spiculation sign is 75-85%, specificity 80-90% [31].

Halo sign – the presence of a ground-glass zone around a solid nodule, reflecting the diffuse spread of tumor cells along the surrounding alveoli [14,32]. The halo sign is often observed in invasive adenocarcinomas, especially those with a lepidic growth component [32].

Vacuole sign – the presence of 2-5 mm gas bubbles within the nodule, reflecting air-containing bronchioles within the tumor or the beginning of cavitation [16,33]. The vacuole sign has high specificity (90-95%) for adenocarcinoma [33].

Cavitation – the presence of a cavity >5 mm within the nodule (necrosis or breakdown) [16,34]. Cavitation is relatively rare in adenocarcinomas (5-10%), but when present, it is often associated with aggressive growth and poor prognosis [34].

Polygonal shape and air bronchogram sign. Polygonal shape – the nodule has a multi-faceted, irregular contour, reflecting tumor growth along surrounding bronchi and vessels [14,16]. Air bronchogram sign – the presence of air-filled bronchi visible within the nodule, a characteristic sign of invasive growth [16].

Pleural retraction sign – the presence of linear opacities (fibrous strands) between the nodule and the pleura, reflecting invasion of the visceral pleura by the tumor or retraction of the pleura by the tumor [14,16].

Diagnostic value of CT semiotic signs. Sensitivity of pure GGO is 85-95%, specificity 70-80% [14,30]. Sensitivity of part-solid GGO is 80-90%, specificity 85-90% [14,30]. Sensitivity of the spiculation sign is 75-85%, specificity 80-90% [16,31]. Sensitivity of the halo sign is 50-70%, specificity 85-95% [14,32]. Sensitivity of the vacuole sign is 40-60%, specificity 90-95% [16,33]. Sensitivity of the air bronchogram sign is 60-75%, specificity 80-85% [14,16]. Sensitivity of the pleural retraction sign is 70-80%, specificity 75-85% [14,16]. The combination of these signs significantly increases diagnostic accuracy. For example, the simultaneous presence of the spiculation sign and vacuole sign has a specificity >95% for adenocarcinoma [16,33].

THE ROLE OF ARTIFICIAL INTELLIGENCE AND DEEP LEARNING MODELS IN CT DIAGNOSTICS

In recent years, the development of artificial intelligence (AI) and deep learning technologies has ushered in a new era in CT diagnostics. These technologies are creating significant opportunities for early detection of lung adenocarcinoma, differentiating histological types, and assessing prognosis [19,40,41].

Convolutional Neural Networks (CNN). Convolutional neural networks (CNN) are the most widely used deep learning architecture for medical image analysis. CNNs enable automatic extraction of important features from images and classification based on them [40,41]. Applications of CNNs in lung adenocarcinoma diagnosis include [40,41,42]: automatic detection of pulmonary nodules; assessment of whether nodules are benign or malignant; differentiation of histological type (adenocarcinoma, squamous cell, small cell); prediction of molecular mutations (EGFR, KRAS, ALK) based on CT images (radiomics).

CNN-LSTM-RF hybrid model. The CNN-LSTM-RF hybrid model developed by Alashban (2026) achieved high results in classifying histological types of lung cancer based on CT images [19]. This model consists of the following components: first – CNN (Convolutional Neural Network) for extracting spatial features from CT images; second – LSTM (Long Short-Term Memory) for modeling sequential (temporal) relationships between CT slices; third – RF (Random Forest) for classifying the LSTM outputs [19]. The main performance metrics of the model are [19]: validation accuracy: 97%; precision: 96%; recall: 96%; F1-score: 98%; AUC: 0.92 to 0.96 (for different classes). This model can distinguish adenocarcinoma, squamous cell carcinoma, and small cell carcinoma from each other with 97% accuracy [19]. This figure is significantly higher than that of experienced radiologists (85-90%).

Radiomics and texture analysis. Radiomics is a method for automatically extracting hundreds or thousands of quantitative features (texture, shape, intensity, fractal dimension, etc.) from CT images and integrating them with clinical data [43,44]. Applications of radiomics in lung adenocarcinoma diagnosis include [43,44,45]: distinguishing histological type (AUC 0.85-0.95); predicting molecular mutations (AUC 0.75-0.85 for EGFR mutation); assessing prognosis (AUC 0.80-0.90 for 5-year survival); predicting immunotherapy effectiveness.

Implementation of artificial intelligence technologies into clinical practice. The implementation of AI technologies into clinical practice offers several advantages [19,40,46]: increased diagnostic speed (analysis of one CT examination may be reduced to 1-2 minutes); reduction of subjective errors (reduces inter-radiologist variability by 30-50%); increased sensitivity for detecting small and early-stage nodules (by 20-30%); reduction of radiologists' workload. However, the implementation of AI technologies into clinical practice also raises several issues [46,47]: the need to adapt models to different CT scanners and protocols; insufficient clinical validation studies; difficulty in interpreting model results ("black box" problem); data privacy and ethical issues.

DIFFERENTIAL DIAGNOSIS

Distinguishing lung adenocarcinoma from other histological types and benign lesions on CT examination is of great clinical importance [48,49,50].

Adenocarcinoma vs. squamous cell carcinoma. Adenocarcinoma is often located peripherally, while squamous cell carcinoma is often located centrally [48]. GGO is frequent (40-60%) in adenocarcinoma,

but rare (5-10%) in squamous cell carcinoma [48]. The spiculation sign is frequent (70-80%) in adenocarcinoma, and moderate (40-50%) in squamous cell carcinoma [48]. Cavitation is rare (5-10%) in adenocarcinoma, but frequent (20-30%) in squamous cell carcinoma [48]. Surrounding lung reaction (obstructive pneumonitis) is rare in adenocarcinoma, but frequent in squamous cell carcinoma [48].

Adenocarcinoma vs. small cell carcinoma. Tumor size varies in adenocarcinoma, while small cell carcinoma is often large (>5 cm) [25]. Lymph nodes are involved sequentially in adenocarcinoma, while small cell carcinoma shows early and massive involvement [25]. Metastases occur late in adenocarcinoma, while small cell carcinoma shows early and widespread metastases [25]. GGO and the spiculation sign are frequent in adenocarcinoma, but rare in small cell carcinoma [48].

Adenocarcinoma vs. benign nodules. Benign nodules (granuloma, hematoma, arteriovenous malformation, hamartoma) differ from adenocarcinoma by the following signs [48,49]: well-defined, smooth margins; uniform, high intensity (calcification, fat); no change or decrease in size over time; absence of spiculation sign; absence of GGO component.

Role of Radiomics in differential diagnosis. Radiomics analysis provides higher accuracy in differential diagnosis compared to traditional visual analysis [43,44,45]. Radiomics can differentiate adenocarcinoma from squamous cell carcinoma (AUC 0.85-0.92), adenocarcinoma from small cell carcinoma (AUC 0.88-0.94), and adenocarcinoma from benign nodules (AUC 0.90-0.95) [45].

PROGNOSIS AND DYNAMIC FOLLOW-UP

CT examination plays an important role in the dynamic follow-up of patients with lung adenocarcinoma, assessment of treatment effectiveness, and early detection of relapse [18,35,51].

Assessment of treatment effectiveness. Changes in tumor size are assessed by CT according to RECIST (Response Evaluation Criteria in Solid Tumors) criteria [51]. Complete remission shows disappearance of all tumor nodules. Partial remission shows a 30% or greater decrease in tumor size. Stable disease shows a state between partial remission and progression. Progression shows a 20% or greater increase in tumor size or appearance of new nodules [51].

Assessment of immunotherapy effectiveness. During immunotherapy (pembrolizumab, nivolumab, etc.), initial tumor enlargement (pseudoprogression) may occur. In this case, repeating CT examination dynamically (at intervals of 4-6 weeks) is important to distinguish true progression from pseudoprogression [52,53].

Early detection of relapse and metastases. In follow-up after treatment, CT examination is recommended at the following intervals [18,35]: Stage I-II (after surgery): every 6-12 months for 5 years; Stage III (after combined treatment): every 3-6 months for 3 years; Stage IV (palliative treatment): every 2-4 months. The sensitivity of CT examination for early detection of relapse and metastases is as follows [18]: local relapse: 85-90%; lung metastases: 90-95%; mediastinal lymph node metastases: 75-85%; distant metastases: 80-90% for CT and 90-95% for PET/CT.

Conclusion

Computed tomography examination has fully confirmed its status as the "gold standard" as the most reliable and effective tool of modern medicine in the diagnosis of lung adenocarcinoma. The early detection capabilities of this technology, particularly low-dose CT (LDCT) screening programs, significantly reduce lung cancer mortality rates (by 20-25%), further emphasizing its clinical importance. The combination of specific CT semiotic signs characteristic of the disease, such as spiculation, halo, vacuole, and pleural retraction, allows clinicians to make an accurate and differential diagnosis. CT-based TNM staging provides high accuracy in assessing tumor size (T), regional lymph nodes (N), and distant metastases (M), enabling correct choice of treatment strategy and prognosis assessment. During technological development, the advent of artificial intelligence and radiomics analysis has elevated diagnostic accuracy to an entirely new level. Automatic analysis of CT images using hybrid neural networks (CNN-LSTM-RF) and deep learning models, as well as predicting molecular mutations through radiomics features, serves as an important foundation for personalizing the treatment process. Such innovative approaches yield high results not only in distinguishing adenocarcinoma from other

histological types (with 97% accuracy) but also in assessing treatment effectiveness (RECIST criteria) and early detection of metastases during dynamic follow-up. The increasing trend of this disease in the Central Asian region, particularly in Uzbekistan, necessitates the widespread implementation of modern diagnostic methods, especially LDCT screening programs. In the future, research should continue in the following directions: studying the genetic characteristics of the Central Asian population; assessing the effectiveness of LDCT screening programs in the region; adapting artificial intelligence models to local CT scanners and protocols; fully integrating radiomics analysis into clinical practice. These measures will be of decisive importance in controlling lung adenocarcinoma and improving treatment outcomes.

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