

Cervical mediastinoscopy in diagnosis and treatment of lung cancer

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Lung cancer remains the leading cause of cancer mortality. It ranks first in the incidence of cancer in the world. According to the European Association of Oncologists, the annual incidence of lung cancer is increasing with every passing year and amounts to about 1.8 million new cases worldwide. Men have a higher prevalence of lung cancer (33.8 per 100,000) than their female counterparts (13.5 per 100,000). In most cases, it is diagnosed at an advanced stage (III–IV), which is characterised by mediastinal lymphadenopathy. Early detection of lung cancer allows seeking early treatment. Lung cancer screening is used to find a tumour and/or lung cancer metastasis, determine its location and size as well as its morphological verification.

OBJECTIVE — to define the most accurate invasive and non-invasive methods of verification and diagnosis of mediastinal lymphadenopathy and improve diagnosis and treatment of lung cancer through the extensive use of cervical mediastinoscopy and creation of an algorithm for its optimal use.

MATERIALS AND METHODS. The study included 146 patients. A wide range of clinical, laboratory, endoscopic (Endobronchial ultrasound transbronchial needle aspiration (EBUS-TBNA), Cervical Mediastinoscopy (CM)), radiographical (Computed tomography (CT), Positron emission tomography (PET)), morphological, immunohistochemical and statistical methods were used. Statistical analysis was performed using Statistics for Windows Version 10.0 (Stat Soft Inc., USA).

RESULTS. The study involved 146 patients who underwent screening for mediastinal lymphadenopathy using mediastinoscopy. According to the laboratory findings, 98 patients had lung cancer. The rest of the cases were presented by other pathologies. Colorectal and stomach cancers were most commonly seen. In one case, the patient had a comorbidity, a combination of lung cancer and colorectal cancer.

CONCLUSIONS. Mediastinoscopy is the most effective diagnostic method for mediastinal lymphadenopathy, especially in lung cancer.

KEYWORDS

mediastinoscopy, lung cancer, mediastinal lymphadenopathy.

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Cervical mediastinoscopy can be described as an invasive method that is used to examine the superior and middle mediastinum for staging of lung cancer and histological investigation of any mediastinal masses of unknown aetiology [2]. It was first described by Carlen in 1959 and is still used today to assess the size of mediastinal nodes observed on the CT-scan images and the stage of carcinoma [1, 7]. Cervical mediastinoscopy helped visualize subcarinal, upper and lower paratracheal lymph nodes. Three groups of lymph nodes were taken for biopsy

[5]. The procedure has a low risk of significant complications, estimated at around 0.5% within the most effective series. The most common complication is an iatrogenic injury to the major vessels. Other reported complications include pneumothorax, left recurrent cartilaginous structure nerve paralysis, tracheal or esophageal rupture, wound infection and profuse haemorrhage. Thoracic CT-scan usually shows enlarged lymph nodes. It is primarily used for non-invasive N-staging. Imaging techniques, among them CT-scan, can't help define a type of tumour,

whether it is benign or malignant, as enlarged lymph nodes could additionally be inflammatory, whereas normal-sized lymph nodes might contain malignancy [4]. CT-scan alongside with mediastinoscopy (with biopsy) and endoscopic ultrasonography (EUS)-guided fine needle aspiration (FNA) biopsy, transbronchial needle aspiration (TBNA) diagnostic assay, and CT guided transthoracic FNA diagnostic assay are widely-used procedures for tissue confirmation, with variable yields and complications [13]. According to the data published by the European Association of Oncology, about 1.6 million new cases of lung cancer are diagnosed annually worldwide [10]. Men have a higher prevalence of lung cancer (33.8 per 100,000) than their female counterparts (13.5 per 100,000) [3]. Early diagnosis is essential for successful treatment of this pathology as it allows patients receive early and personalized treatment [8]. Cancer diagnosis includes investigation of the tumour, its location, size, spread, and morphological verification [14]. The most common non-invasive methods include laboratory examinations, chest radiography, magnetic resonance imaging (MRI), computerized tomography (CT), PET/CT, osteoscintigraphy, which may show the presence, development and localization of the oncological growth. These procedures are applied as a primary stage of diagnostic process and help choose an appropriate invasive technique for morphological verification [9, 11, 16]. Accurate diagnosis of lung cancer requires a range of invasive procedures such as transthoracic puncture biopsy, fibrobronchoscopy with biopsy, transbronchial biopsy (EBUS TBNA), transesophageal biopsy (EUS-FNA), video thoracoscopy with biopsy, cervical mediastinoscopy (CM), and open biopsy [12, 15].

OBJECTIVE – to define the most accurate invasive and non-invasive methods of verification and diagnosis of mediastinal lymphadenopathy and improve diagnosis and treatment of lung cancer through the extensive use of cervical mediastinoscopy and creation of an algorithm for its optimal use.

Materials and methods

The study was conducted at the Oncology clinic of the Department of Oncology of Bogomolets National Medical University (Kyiv, Ukraine) and at Kyiv Clinical Railway Transport Hospital No. 3 from 2016 to 2021. The study involved 146 patients who underwent screening for mediastinal lymphadenopathy using mediastinoscopy. A wide range of clinical, laboratory, endoscopic (Endobronchial ultrasound transbronchial needle aspiration (EBUS-TBNA), Cervical Mediastinoscopy (CM)),

radiographical (Computed tomography (CT), Positron emission tomography (PET)), morphological, immunohistochemical and statistical methods were used. Enlarged mediastinal lymph nodes seen on the CT-scan image was an indication for mediastinoscopy. Mediastinoscopy was performed under general anaesthesia, with a patient lying on their back and a roller beneath their shoulders. The first anatomical landmark was a jugular notch, above which a skin incision was created within the lower third of the neck in the transversal direction. The second anatomical landmark was a trachea. After dissection of the pretracheal fascia, the trachea was exposed, and the forefinger was inserted into the wound canal, the paratracheal tissue was stratified, and a mediastinoscope was inserted. The third anatomical landmark is a tracheal bifurcation. Paratracheal areas, tracheal bifurcation, and the main bronchi were examined. Enlarged lymph nodes were taken for excision biopsy from different sites. Patients were discharged from the hospital on the day of surgery or the following day.

The study was conducted according to the provisions of the Helsinki Declaration of Human Rights, and every participant gave their written informed consent.

Statistical analysis was performed using Statistics for Windows Version 10.0 (Stat Soft INC., USA). Parameters are given within the form $M \pm m$, where M is an average value, m is the standard deviation. In the case of $p < 0.05$, variations were set as statistically significant.

Results and discussion

The study involved 146 patients who underwent screening for mediastinal lymphadenopathy using mediastinoscopy. According to the laboratory findings, 98 patients had lung cancer. The rest of the cases were presented by other pathologies. Colorectal and stomach cancers were most commonly observed. In one case, the patient had a comorbidity, a combination of lung cancer and colorectal cancer.

The inspection of enlarged lymph nodes allowed discovering of their different combinations. In the majority of cases, the samples of three groups of lymph nodes were taken. (Table 1). Cervical mediastinoscopy was primarily used for N-staging in patients with carcinoma. The sensitivity of CT-scan was 97.6% – (95%CI [89.3–100.0]). Additionally, a reliable specificity indicator was established at 46.5 (95% CI [32.3–61.2]) and a low probability of false-negative rate – 0.05 (95% CI [0.01–0.26]). (Table 2). To compare CT-scan with mediastinoscopy, lung resection with lymph node dissection

Table 1. The ratio of different combinations in affected lymph nodes in patients with lung cancer

Parameter	Cases, %
2R, 4R, 7	18,38
4R, 4L, 7	21,5
4L, 7	9,3
2R, 4R	7,73
4R, 4L	5,2
4R	9,12
2R, 4R, 4L, 7	2,62
2R	2,83
2R, 2L, 4R, 4L	3,9
2L, 4L, 10L, 4R	1,26
4R, 7	7,44
2R, 4R, 4L	6,34
4R, 10R	3,38

Table 2. Parameters of diagnostic value of CT-scan compared to the results of histologic investigations in patients with lung cancer who underwent cervical mediastinoscopy

Parameter	Value (95 % CI)
Sensitivity	97.6 (89.3–100.0)
Specificity	46.5 (32.3–61.2)
Youden's index	0.44 (0.31–0.57)
Area under ROC curve	72.1 (65.6–78.6)
Diagnostic odds ratio	36.5 (6.4–97.8)

was performed in 12 cases in patients who underwent preoperative mediastinoscopy. The histological results were consistent in all cases. However, for the determination of sensitivity and specificity, the group is statistically insignificant. Further investigation of more patients is necessary and, therefore, is planned.

According to chest CT-scan, in patients with carcinoma, mediastinal lymph nodes from 10 to 14.9mm were discovered in 78 (54.76 %) patients and 15 mm in 68 (45.24 %) patients. Lung cancer metastases within the mediastinal lymph nodes were detected in 98 (67.12 %) patients. According to the CT-scan data, in 48 (32.87 %) patients, mediastinal pathology was not caused by lung cancer metastasis. The histologic distribution was as follows: squamous cell lung cancer – 23.8 % cases, adenocarcinoma – 57.1 %, small cell carcinoma – 19.04 %. Consistent with the classification, TNM – $T_4N_3M_0$ – 10, $T_4N_2M_0$ – 9, $T_4N_2M_1$ – 6, $T_3N_3M_1$ – 6, $T_3N_2M_0$ – 9, $T_3N_0M_0$ – 9, $T_2N_3M_1$ – 8, $T_2N_3M_0$ – 16, $T_2N_3M_1$ – 3, $T_2N_2M_1$ – 3, $T_2N_0M_0$ – 15, $T_1N_2M_0$ – 4. The results of the surgical histologic examination of mediastinal lymph nodes coincided with the histologic results of operative cervical mediastinoscopy in all cases (100.0 [97.1–100.0]). False negative rate zero.01 [0.25–2.89] was unreliable. Cervical mediastinoscopy influenced the selection of treatment techniques.

Cervical mediastinoscopy is a safe, accurate and cost-effective procedure that minimizes hospital stays and initiates adequate treatment immediately after receiving the results of histopathological examination. The main advantage of this technique is its high diagnostic value – sensitivity is about 81.8 %, and specificity – 100 %. This technique allows sampling of morphological material sufficient to perform a histologic, immunohistochemical and molecular investigation that makes it possible to diagnose a disease and prescribe treatment objectively. Histologic analysis of mediastinal lymph nodes is feasible after using invasive diagnostic strategies like VATS, EBUS-TBNA, and cervical mediastinoscopy. The disadvantages of VATS are often thought of as invasiveness of the technique, the ability to perform only unilateral diagnostic test of lymph nodes, and a long hospital stay. The disadvantages of EBUS-TBNA are expensive equipment and the ability to perform diagnostic tests of a limited quantity of the material. N-staging of carcinoma could be a significant indication for mediastinoscopy. The most significant advantage of mediastinoscopy over other procedures is that this technique provides morphological confirmation of the tumour spread. However, the study suggests that chest CT-scan cannot be used as a complete technique for carcinoma staging. The method detects mediastinal lymph nodes accurately only in 52–58 % of cases. A CT-scan shows any affected lymph nodes larger than 1 cm. However, the frequency of false positives is more or less half-hour. According to the results of modern studies, on average, the sensitivity and

specificity of chest CT of intrathoracic lymph nodes metastases of carcinoma is 56–63% and 52.75%, severally, whereas, with mediastinoscopy, these indicators reach 98–100% and 95–97%, severally. In terms of sensitivity and specificity (80% and 96–98%, respectively), positron emission imaging approaches mediastinoscopy. Mediastinoscopy remains the most effective diagnostic investigation of choice for mediastinal pathology, especially in lung cancer [18].

Conclusions

Cervical mediastinoscopy in patients with primary lung cancer helps establish a reason for the enlargement of mediastinal lymph nodes and verify the frequency of various combinations in the study groups as well as verify diagnosis and N status in all cases.

The sensitivity of CT was 97.6% – (95%CI [89.3–100.0]). The reliable specificity was 46.5 (95% CI [32.3–61.2]) and probability of false-negative rate – 0.05 (95% CI [0.01–0.26]).

The results of operative microscopic anatomy examination of the mediastinal lymph nodes coincided with the histologic results of surgical cervical mediastinoscopy in all cases (100.0 [97.0–100.0]). False-negative rate 0.01 [0.25–2.89] was unreliable.

Cervical mediastinoscopy makes it possible to get enough tissue samples for immunohistochemical study to establish accurate diagnosis and prescribe proper treatment for patients with primary lung cancer.

DECLARATION OF INTERESTS

The authors declare no conflicts of interest.

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AUTHOR CONTRIBUTIONS

R. Vereshchako: a study concept and design, critical review, final approval of the article; O. Piskorskyi: data collection and analysis, statistical analysis, writing the article; I. Sukhin: data collection and analysis, critical review.

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Роль шийної медіастиноскопії у діагностиці та лікуванні раку легень

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Рак легень залишається основною причиною смерті від раку. Він посідає перше місце за захворюваністю на рак у світі. За даними Європейської асоціації онкологів, захворюваність на рак легень зростає. Щороку у світі реєструють близько 1,8 млн нових випадків раку легень. Чоловіки хворіють частіше, ніж жінки (відповідно 33,8 і 13,5 випадку на 100 тис. населення). Більшість діагностованих випадків припадає на III—IV стадії, для яких характерна медіастинальна лімфаденопатія. Рання діагностика дає змогу розпочати своєчасне лікування. Основним завданням діагностики раку легень є визначення локалізації, розмірів, поширення та морфологічна верифікація пухлини.

Мета — визначити найточніші інвазивні та неінвазивні методи верифікації і діагностики медіастинальної лімфаденопатії та поліпшити результати діагностики і лікування раку легень шляхом широкого застосування шийної медіастиноскопії та створення алгоритму її оптимального використання.

Матеріали та методи. У дослідження було залучено 146 пацієнтів. Використано загальноклінічні, лабораторні, ендоскопічні (ендобронхіальна ультразвукова трансbronхіальна голчаста аспірація (EBUS-TBNA), шийна медіастиноскопія), рентгенографічні (комп'ютерна томографія, позитронно-емісійна томографія), морфологічні, імуногістохімічні та статистичні методи дослідження. Для аналізу статистичних даних застосовували програму Statistics for Windows Version 10.0 (Stat Soft Inc., США).

Результати. Усім хворим виконано медіастиноскопію. У 98 діагностовано рак легень. Решта випадків були представлені іншими патологіями. Найчастіше виявляли колоректальний рак і рак шлунка. В одному випадку у пацієнта була супутня хвороба, поєднання раку легень та колоректального раку.

Висновки. Медіастиноскопія є найефективнішим методом діагностики лімфаденопатії середостіння, особливо для хворих на рак легень.

Ключові слова: медіастиноскопія, рак легень, медіастинальна лімфаденопатія.

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