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Main topics of I-ELCAP protocol – the International Early Lung Cancer Action Program

The International Early Lung Cancer Action Program (I-ELCAP) aims to promote early diagnosis and treatment of lung cancer. I-ELCAP international protocol underlies all national screening programs around the world.

Keywords: *early lung cancer, International Early Lung Cancer Action Program, I-ELCAP.*

The International Early Lung Cancer Action Program (I-ELCAP) has developed and implemented the protocol of early lung cancer detection that was approved by the Office of Health Promotion Research, USA. The protocol was developed by one of the I-ELCAP founders, Professor Claudia Henske [1, 2, 3]. The geography of the I-ELCAP program is very broad, and today this protocol underlies the national screening programs around the world.

The scientific teams – participants of I-ELCAP program, should strictly follow the I-ELCAP protocol, which includes primary or baseline screening and frequency of rescreening, which depends on the nature of pulmonary node detected during the primary baseline screening. The pulmonary node growth is assessed in dynamics in percent. The main requirement is to perform a primary LDCT chest scanning and at least one repeated screening [4,5]. The participation of scientists from Kazakhstan in the program and implementation of the protocol should be agreed with the Program administrators.

In addition, the I-ELCAP policy is aimed at continued monitoring of all node-positive patients with confirmed diagnosis of "lung cancer" for at least 10 consecutive years. For higher confidence, the I-ELCAP compiles the database for each participating organization, in which the results of baseline and all subsequent screenings are fully documented. It is also very important to identify and document all cases of temporary diagnosis of lung cancer in all screened patients, indicating the reason for terminating the screening [4].

The ELCAP is improving the protocol for over ten years [5, 6]. The protocol was revised in the framework of the International Conferences organized by the ELCAP group 2 times a year. The I-ELCAP research program is governed by a common protocol [7] and is aimed at a long-term perspective of ongoing screening. The latest updated version of protocol was developed based on in-depth understanding of all aspects of the disease [7, 8].

The structure of the I-ELCAP protocol provides an opportunity for performance of interrelated supportive examinations: various non-CT studies (e.g., saliva, blood, urine), which could be carried out in parallel with LDCT. It ensures the study of respective merits and estimation of the screening cost: cost of CT scan separately and in combination with additional examination methods [1-6].

The early lung cancer protocol for Kazakhstan KZ-ELCAP was approved by I-ELCAP and the Office of Health Promotion Research (USA) experts for its introduction and implementation in the Republic of Kazakhstan. Besides, the ELCAP protocol was approved by the Local scientific ethics committee of the "National Research Cardiac Surgery Center" JSC.

The KZ-ELCAP protocol was successfully implemented in Kazakhstan within the grant research "Early lung cancer diagnostics", jointly by the scientific team of "National Research Cardiac Surgery Center" JSC and Oncology Center of Astana city, Republican State Enterprise on the Right of Economic Activity (RSE REA).

The research findings were published in Kazakhstani and international peer-reviewed publications, and presented at the Annual I-ELCAP Conference "33rd International Lung Cancer Screening Conference and the 1st International Conference on Early Lung Cancer Treatment", held on December 4-5 at the Mount Sinai Clinic of Jahan Medical School, New York, USA.

This article presents the analysis of main issues of the last version of protocol, adapted for implementation in clinics of Kazakhstan. The informative and detailed protocol contains the description of work of all participants within the research.

Main topics of I-ELCAP protocol. Computed tomography (CT)-images obtained at all stages of baseline and/or repeated screening are compared to the initial low-dose computed tomography (LDCT) images to identify all visible non-calcific nodes.

The central non-transparent node of non-linear character can be "solid", "partially solid" or "non-solid" (the latter two have the "diffusing glass" transparency), and is located in the parenchyma or endobronchial region.

A node is classified as "non-calcific" if it does comply with the common criteria of a calcifying benign node.

The node less than 5 mm in diameter is considered as non-calcific if its density is less than the rib density.

The node of 5-20 mm in diameter is non-calcific if its major part was not calcific and/or calcifying, but did not comply with the classical pattern of a calcifying benign formation, and/or had "spicular" edges.

The node of over 20 mm in diameter is non-calcific if any of its part is not calcific (according to the above specified criteria) [6-8].

The mean size of the length and width is considered the node diameter. The length is measured on one CT-image, where the node maximum length is determined; the width is defined as the longest perpendicular to the node length, measured on the same CT-image.

The changes in other thoracic organs, including mediastinum, heart, soft tissues and bones, are also documented.

The mediastinal mass are tumours originating from the mediastinum, including the thymus, heart and esophagus, as well as the thyroid gland tumours extended into the mediastinum. The mediastinal mass and soft tissues tumours are registered in reference to their location and size. The radiologist also documents the visualization of the upper abdomen part with respect to the location and size.

Each coronary artery is identified: main (principal), left anterior descending, circumflex and right arteries. The confirmed calcification in each artery is registered as "no calcification", or "minimal", "moderate", or "marked". The calcification is graded on the scale from 0 to 3. The "minimal" grade is determined - if less than 1/3 of the entire artery length was calcified, "moderate"- if 1/3 – 2/3 of the entire artery length was calcified, and "marked"- if over 2/3 of the entire artery length is calcified.

The protocol includes the identification of the emphysema degree, which can be defined as "no emphysema", "minimal", "moderate", or "marked". Each degree is graded from 0 to 3 [4, 6, 7].

The screening frequency is determined by the result of baseline CT screening: if the CT screening did not reveal a cancer process, the second CT screening should be repeated after 1 year.

If lung cancer (LC) was diagnosed at stages I, II or IIIA, the patient should participate in screening according to the set schedule, after the interventional procedures.

The researchers are called upon to follow the annual screening protocol. It is not recommended to introduce any changes into the specified interval, since the single screening frequency is required for generalization of the multicentre study results [4, 7, 8, 9].

Baseline (initial) screening: The CT-study is considered as "positive" if at least one "solid", "partially solid" or "endobronchial" node of 5.0 mm or more in diameter is found.

If non-calcific nodes are detected, but all of them of too small size to suspect the positive findings, including a non-solid node of any size, the result is regarded as the semi-positive, and the patient has to undergo the LDCT study 12 months after the initial screening.

If no nodes were found and the test was negative, the patient is subject to a repeated CT after 12 months.

In case of detection of "solid" and "partially solid" node of 5 to 15 mm size, the patient should undergo the repeated LDCT after 3 months.

If the node showed the malignant growth (according to the growth assessment scale), the biopsy examination is prescribed.

If there is no growth, or the node is partially or completely resolved, the study is discontinued.

In case of negative or undefined biopsy result, the LDCT is prescribed after 3 months.

In case of multiple nodes and suspect to latent infection or inflammation, the course of broad-spectrum antibiotics with anaerobic effect is prescribed, followed by the LDCT scanning after 3 months.

For "solid" and "partially solid" nodes of 15 mm or more in diameter, with suspected cancerous nature, the biopsy examination of the node is prescribed.

In case of suspected latent infection, the course of antibiotic therapy with anaerobic effect is prescribed followed by LDCT examination after 1 month.

If repeated LDCT did not show the node's resolution or the level of malignancy is maintained, the node biopsy is prescribed.

If the biopsy examination did not reveal the lung cancer, the repeated CT-screening is performed in 12 months after the first baseline CT examination [7, 9].

Repeated (annual) screening includes compulsory review of the original CT-image that should identify all non-calcific nodes regardless of the size, with special focus on the node(s).

The focus is directed to those nodes that show growth starting from previous screening, of the whole size or the size of solid component detected earlier, or the detection of the solid component in previously non-solid node.

Within repeated screening, the results of LDCT are considered as positive if at least one non-calcific solid or partially solid node with the size of 3 mm or endo-bronchial node with the size of 5.0 mm in diameter of temporary growth was identified. If the new solid or partially solid node was found of the size less than 3 mm or the non-solid node component of any size, the result should be considered as the semi-positive, with prescribed CT screening in 12 months. If the test was negative, the second CT screening should be carried out in 12 months.

In case of detection of non-calcific nodes, and all of them are too small to suspect the positive result, including the non-solid node of any size, the result is regarded as the semi-positive with assigned LDCT in 12 months after the baseline screening.

If the node was not identified, the test should be regarded as the negative with prescribed repeated CT scanning in 12 months.

In case of detection of solid and partially solid node of 5 to 15 mm size, the repeated LDCT is prescribed in 3 months. If the node showed malignant growth (according to the growth assessment scale), the biopsy examination is prescribed. If there is no growth or the node is partially or completely resolved, the study is discontinued.

In case of multiple nodes and suspect to latent infection or inflammation, the course of broad-spectrum antibiotics with anaerobic effect is prescribed, followed by the LDCT scanning in 3 months.

For "solid" and "partially solid" nodes of 15 mm in diameter, the biopsy examination of the node is prescribed.

In case of suspected latent infection, the course of antibiotic therapy with anaerobic effect is prescribed, followed by LDCT examination in 1 month.

If repeated LDCT did not show the node's resolution or the level of malignancy is maintained, the node biopsy is prescribed.

If the biopsy examination did not reveal the lung cancer, the repeated CT-screening is performed in 12 months after the first baseline CT examination.

For all patients of the study with discontinued diagnostic algorithm or with no lung cancer according to the biopsy findings, the second CT screening is performed 12 months after the initial baseline examination [4, 7, 9, 10].

The node growth assessment: a) The growth of the node is determined by increasing or expansion of the node size and/or the "solid" component, "partially solid" node, and/or developing of the "solid" component in non-solid node at subsequent CT scan after the baseline repeated annual CT examination; b) The volume doubling rate assessment, based on measuring of the node size in two specific views. The time between these two views should be adequate for generation of significant detectable changes in the node volume.

The criteria for significant changes (in percentage) of the node diameter or the "solid" component growth in the "partially solid" node: a) for the node <5 mm in diameter – for at least 50%; b) for the node 5-9 mm in diameter – for at least 30%; c) for the node > 10 mm in diameter – for at least 20% [4, 6, 8, 10].

The trans-thoracic fine needle biopsy (TTFNB) is performed in patients with nodes > 8 mm. The TTFNB procedure is carried out under the CT control in outpatient settings with provision of local anaesthesia by one needle puncture.

Samples obtained by TTFNB undergo cytological testing to confirm LC diagnosis by histomorphologic identification of the form of cancer. The images from cytological examination of samples are computerized for further description and classification [7, 10, 11].

Biopsy samples are described and classified according to the standard diagnostic categories.

If the CT-biopsy is not feasible, biopsy with ultrasound guidance, or bronchoscopic biopsy is recommended for patients.

The diagnosis of "lung cancer" is considered to be based on screening diagnostics in case of positive results of baseline CT, regardless of when the diagnosis was really established. The diagnosis is classified as the "lung cancer" in case if the baseline screening revealed the "semi-positive" result, and repeated CT in 12 months detected at least one non-calcific node. If the result of initial CT screening was negative, but the diagnostic examinations showed suspicious findings before the planned annual baseline screening, the diagnosis should be classified as the "temporary LC diagnosis"[12, 13].

Conclusion. Multi-year studies of the I-ELCAP international team have demonstrated the applicability of the I-ELCAP protocol in broad clinical practice.

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