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International Association for the Study of Lung Cancer, American Thoracic Society, and European Respiratory Society recommendations on the microscopic classification of lung adenocarcinoma.

Zalecenia dotyczące mikroskopowej klasyfikacji raka gruczołowego płuca przedstawione przez *International Association for the Study of Lung Cancer*, *American Thoracic Society* i *European Respiratory Society*

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In February 2011 ample recommendations concerning the new classification of primary lung adenocarcinoma and the diagnostic evaluation of small biopsies and cytology specimens were published [1]. The recommendations are the result of several years of multidisciplinary research conducted by various experts: oncologists, pneumonologists, thoracic surgeons, radiologists, pathologists, and molecular biologists and based on large groups of patients.

Previously the stage of the disease was the main prognostic factor in lung cancer. It was also essential to establish whether the patient had small-cell or non-small cell lung carcinoma (NSCLC), while the subtype of NSCLC, particularly in the case of unresectable NSCLC, was not important, as it did not affect the management.

The gradual evolution of knowledge on the molecular and genetic bases of lung cancer and the introduction of new treatments dramatically changed the approach to the diagnosis and classification of NSCLC, especially primary adenocarcinoma (ADC).

The aim of the recommendations was to emphasise the prognostic and predictive values of the proposed classification of ADC and the significance of the morphological type of the cancer in the selection of treatment and its efficacy.

These recommendations contain precise histological criteria for the identified types of primary adenocarcinoma and provide an algorithm for the diagnostic evaluation of small biopsies and cytology specimens.

Evaluation of postoperative material requires the testing of many fragments of the tumour and provision of information on the predominant histology and on the presence of additional morphological types of ADC, preferably with determination of the percentage contribution of each type.

New concepts are introduced in the recommendations: adenocarcinoma in situ (AIS), which corresponds to tumours previously referred to as solitary bronchioloalveolar carcinoma, (BAC) and minimally invasive carcinoma (MIC), emphasising the very favourable prognosis in these two cases.

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The recommendations provide the first classification of adenocarcinomas previously referred to as BAC. Despite the morphological criteria introduced by the World Health Organisation (WHO) in 1999 [2] and then in 2004 in the classification of the „Tumours of the lung, pleura, thymus, and heart” [3] the diagnosis of BAC referred both to the solitary tumour and to multiple tumours although these two types differ in terms of biology, clinical course, and prognosis. The new recommendations no longer use the term ‘bronchioloalveolar carcinoma’. It has been replaced by the term ‘AIS’ for the solitary type and ‘lepidic predominant ADC’ for the disseminated type.

The recommendations introduce new histological subtypes of ADC, discontinuing the less common forms or moving them to other subgroups. The diversity of the morphological types of ADC is of considerable importance, as it allows prediction of the presence of mutations in the tumour cells. Cancers with lepidic, papillary, or micropapillary histology more commonly demonstrate EGFR (epidermal growth factor receptor) mutations, while tumours with mucinous histology are usually associated with the *KRAS* (Kirsten rat sarcoma viral oncogene homologue) gene mutation or with the presence of the *ALK* fusion gene.

In more than 70% of lung cancer cases the diagnosis is based on biopsies and cytology specimens, in which it is not always possible to find histological features that would allow the tumour type to be established. It has therefore become necessary to develop a unified strategy for the handling of small biopsies and/or cytology specimens to unify the diagnostic criteria.

The new recommendations emphasise the significance of sparing use of the collected material, both biopsies and cytology specimens, as it is used not only for pathological diagnosis but also for molecular evaluation that is necessary to determine potential mutations which determine the choice of appropriate treatment.

Currently in cases of unresectable NSCLC every effort should be made to determine the subtype of the tumour and to differentiate adenocarcinoma from squamous cell carcinoma. For this purpose, in cases in which no morphological features are identified that would enable determination of the NSCLC subtype, it is necessary to carry out additional histochemical staining and, most of all, immunohistochemical (IHC) reactions to allow microscopic diagnosis to be established or approximated.

IHC staining has become an integral element of the diagnosis of lung cancer, both in the NSCLC subtype determination and in the differentiation between primary and metastatic tumours. The necessity to

expand the histological diagnosis results in a longer turnaround time and increased cost of testing. In order to avoid the unnecessary costs, collaboration between the clinician and the pathologist evaluating the material is of the utmost importance. Precise information on the stage of the tumour is necessary. In patients with resectable cancer, additional investigations do not need to be performed as the type of NSCLC does not affect further management in these cases.

Differentiation between primary adenocarcinoma and a metastatic tumour is another problem, and it usually requires the inclusion of IHC in the array of diagnostic methods.

Due to the necessity to use the collected material sparingly and to perform only the necessary staining to establish the diagnosis, clinical details of the cancer are essential.

The new recommendations reflect the enormous changes that are happening in terms of approach to the treatment and histopathological diagnosis of primary lung cancer. They emphasise the highly important role of microscopy in the selection of appropriate therapy. For the first time the detailed recommendations regarding the handling of small biopsies and cytology specimens and regarding the use of IHC to establish the diagnosis have been simplified.

Currently, any facility that diagnoses lung cancer cannot function without the possibility of performing additional staining, in particular IHC.

The new recommendations raise the significance of creating interdisciplinary teams based on specialist facilities that are concerned with the diagnosis and treatment of lung cancer and that use microscopy, including IHC, for the assessment of mutations and for selection of treatment.

The new recommendations are without a doubt an enormous breakthrough in the approach to primary lung cancer and, as the authors emphasise, further research is necessary to enable the evaluation of the usefulness of the proposed changes.

Conflict of interest

The authors do not report any conflict of interest.

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