

EJPMR

**EUROPEAN JOURNAL PHARMACEUTICAL
AND MEDICAL RESEARCH**



Published by
Editor in Chief
EJPMR

**MORPHOLOGICAL CHARACTERISTICS OF METHODS FOR ASSESSING KI-67 IN
INFILTRATING BREAST CANCER**

Alimhodzhaeva L.T.*, Zakirova L.T., Nishanov D.A., Khodjaev A.V., Norbekov M.Kh., Nigmanova N.A.,
Zakhirov N.N.

Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology of the Ministry of Health
of the Republic of Uzbekistan Tashkent.

*Corresponding Author: Alimhodzhaeva L.T.

Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology of the Ministry of Health of the Republic of
Uzbekistan Tashkent.

Article Received on 01/01/2019

Article Revised on 22/01/2019

Article Accepted on 12/02/2019

TOPICALITY

The problem of breast cancer (BC) is relevant for modern oncology, which is associated with a pronounced increase in the incidence of women with this pathology and the search for new ways of treatment, in particular the widespread introduction of cost-effective surgical interventions, new antitumor and hormonal drugs. Historically, breast cancer was considered as a single disease. The development of science allowed us to first isolate hormone-dependent tumors into a separate group, then divide tumors according to HER2 status, and then isolate tumors that have virtually none of the three estrogen receptor markers, progesterone receptors and HER2 receptor overexpression. Depending on the allocation of a particular subgroup of breast cancer, treatment approaches change. The Ki67 marker allows determining the "hidden" proliferative potential of a tumor and judging the degree of malignancy. An indicator of less than 10% - the prediction of survival is 95%. With the result from 10 to 15% - the five-year boundary is successfully overcome by 85% of patients. Norm Ki67 for breast cancer is up to 15%, at which the prognosis is favorable. The purpose of treatment with hormonal drugs is shown. Pr 30%-carcinoma will respond well to chemotherapy. The result of 90% - pronoz unfavorable, the survival rate is almost zero. It has been experimentally proven that with carcinoma sensitivity to hormonal drugs and the absence of secondary lesions in other organs and lymph nodes, but with high Ki67 rates, the likelihood of recurrence is very high. If, at a relapse of the disease, the Ki67 values were higher in the first tumor, then the secondary new formation is more aggressive. Therefore, it will require the appointment of a combined treatment.

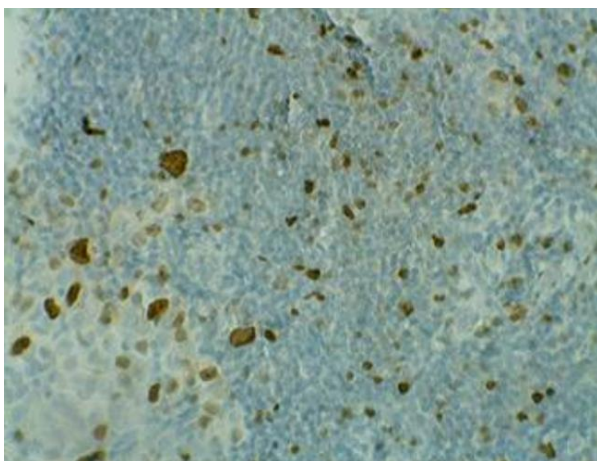


Fig.1: Carcinoma of the breast. IHCh reaction Ki67 25%. ×200.

To assess the proliferative assessment of a tumor in clinical practice, the mitotic index measured by the histological preparation and the Ki-67 index in the preparation stained with an immunohistochemical method are considered the most studied. These methods have certain limitations and if the assessment of the

mitotic index is firmly included in the classification diagnostic schemes, then when defining the Ki-67 index, repeated attempts to standardize the methodological and technological approaches always led to the conclusion that the assessment methodology needed validation in planned clinical studies large studies with a sufficient number of laboratories. The introduction of quantitative evaluation instead of the traditionally accepted semi-quantitative scoring system is always a critical stage in the application of the method. The introduction of the IPA Ki-67 with the obligatory assessment of the percentage of positively stained cells in the daily practice of the pathology department is associated with the problem of reproducing the quantitative assessment of IPA. As a surrogate marker, IPA is used to separate the ER – positive luminal A and B subtypes of breast cancer. The threshold level of separation of IPA between these two groups is considered to be 30%, where, respectively, the luminal type A contains less than 40% of Ki-67 - positive cells, the luminal type B - more than 90% of Ki-67 positive cells. In addition, a threshold level of Ki-67 index above 20% is considered important for administering adjuvant chemotherapy for the luminal B, but not the luminal A subtype of a breast tumor. In

connection with the development of digital imaging methods in morphology, new methods are proposed for evaluating IPA using digital image analysis of scans of histological specimens. It is believed that the automatic analysis of the Ki-67 index is a method that can replace the visual assessment of the IPA and improve accuracy and reproduction.

The aim of the study is to compare two methods of IPA research: a visual method and digital analysis, to study the distribution of IPA Ki-67 by type of material.

MATERIAL AND METHODS

The study of the Ki-67 index was carried out in the laboratory of Pathomorphology of RSSPMCOR of the Ministry of Health of the Republic of Uzbekistan 104 cases of infiltrative breast cancer were analyzed according to the degree of malignancy G2-G3. Fixed in neutral 10% formalin, paraffin-embedded breast tumor material was subjected to a standard morphological study with an assessment of the degree of histological malignancy, followed by an IHC study.

RESULTS AND DISCUSSION

The median IPA for the analyzed material, according to the data was 25.7%. The distribution of IPA in all groups was close to bimodal. The degree of malignancy G2-G3 IPA showed high values, especially in group 1 of the study. The median obtained in the range of 10-37% of IPA is in the range from 21 to 27%. This interval represents only a quarter of the total number of cases investigated. The intraclass ICC coefficient between the digital and visual analysis methods showed a strong correlation within the gray zone. Statistical processing of Ki-67 index data obtained as a result of a visual assessment showed a positive correlation. The distribution of IPA in the digital analysis group revealed the presence of a gray zone of 10-35% of IPA, which indicates that the threshold of 14-20% of IPA for distinguishing between luminal-A and luminal-B subtypes of the mammary gland tumor is within the gray zone. The data obtained indicate that digital analysis can serve as one of the methods of standardization of the IPA study in the proposed border of up to 37% and is important for control.

CONCLUSION

The distribution of IPA with the digital method of analysis confirmed the boundaries of the gray zone from 10 to 37% with a median of 24%. Within these limits, there was a lack of reproducibility between studies with a visual method of analysis. The values of the IPA above and below the border of 10-37% showed sufficiently high level of reproducibility. Based on the data obtained, it can be concluded that digital analysis of research is one of the most acceptable and accurate methods of monitoring the effectiveness of breast cancer treatment.

REFERENCES

1. Jones P.A., Baylin S.B. The fundamental role of epigenetic events in cancer // *Nat. Rev. Genet.*, 2002; 3: 415-428.
2. Baylin S.B., Esteller M., Rountree M.R. Aberrant pattern of DNA methylation, chromatin and gene expression in cancer// *Hum. Mol. Genet.*, 2001; 10: 687-692-696.
3. Esteller M. Epigenetics in cancer // *N. Engl. J. Med.*, 2008; 358: 1148-1159.
4. Chan A.O., Kim S.G., Bedeir A. et al. CpG island methylation in carcinoid and pancreatic endocrine tumors// *Oncogene*, 2003; 13: 924-934.
5. Jones P.A., Baylin S.B. The fundamental role of epigenetic events in cancer // *Nat. Rev. Genet.*, 2002; 3: 415-428.
6. Fraga M.F., Esteller M. Hypermethylation of tumor-suppressing gene and diagnostics of oncological disease//*Cancer*, 2009; 45: 234-239.