論 文 要 旨

Ki-67 is a strong prognostic marker of non-small cell lung cancer when tissue heterogeneity is considered

田畑　和宏

Background: Ki-67 expression is a well-established prognostic marker in various cancers. However, Ki-67 expression is also known as being heterogeneous. We investigated the prognostic significance of Ki-67 from the view of staining heterogeneity by the technique of Spiral Array.

Methods: 100 cases of resected lung cancer from Toyama university hospital archive were collected. Spiral Array blocks were generated out of 100 cases using 100 μm thick paraffin sections. Four μm thick sections of the Array block were stained for Ki-67. Staining results in each reel were scored for areas with lowest (LS), highest (HS), and average (AS) expression, exclusively in the cancer cells. Heterogeneity score (HeS) was designed as the difference between HS and LS. The scores were divided into four grades (0–3). Clinical information was collected, and the prognostic significance of Ki-67 was analyzed.

Results: Pathological stage was available for 91 patients (43 stage IA, 22 stage IB, 2 stage IIA, 9 stage IIB, 13 stage IIIA, 1 stage IIIB, and 1 stage IV). The HS of Ki-67 score in non-small cell lung cancer was 3 in 17 cases, 2 in 27 cases, 1 in 28 cases, 0 in 21 cases, and 4 reels were lost. 78 cases had clinical follow up. 74 cases had all the information available and were analyzed for correlation between Ki-67 expression and survival. Cases with score 2 and 3 of HS and HeS showed significant poorer prognosis (both $P < 0.001$), whereas LS or AS did not show significance. The results were identical when analyzing adenocarcinoma and squamous cell carcinoma, separately. Cox multivariate analysis of Ki-67 showed that HS was an independent risk factor affecting overall survival.

Conclusions: Ki-67 is a strong prognostic marker for non-small cell lung cancer when the degree of highest staining frequency or heterogeneity is considered.

Additional comment: In UICC 7th revision, it is defined that the case with pulmonary metastasis in the same lobe of original tumor is categorized into pathological T3 (pT3). In additional file 1, the category of pm1 (presence of pulmonary metastasis in same lobe of original tumor) included 23 cases, but pT3 included 10 cases only. We could not confirm the medical records of cases, because we had formed this cohort anonymized on collecting it. There might not be significant differences of the parameters, including presence of metastasis, pathological T factor, and pathological stage, with the Ki-67 scoring in our analyses, but we consider that Ki-67 is still strong prognostic marker of non-small cell lung cancer.