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Letters

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The Prognostic Value of Cell Proliferation in Non-small Cell Lung Cancer Assessed with Tritiated Thymidine and Anti-PCNA Antibodies

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THE PROGNOSTIC significance of thymidine and PCNA labelling index (T-LI and PCNA-LI) was studied in 38 patients with operable non-small cell lung cancer (NSCLC) and with a follow-up period from 3 to 6 years after surgery.

In all cases, several tissue fragments were removed from the central and peripheral zones of the tumour. For each sample, proliferative activity was assessed both by autoradiography with tritiated thymidine, and by immunohistochemistry with anti-PCNA antibodies.

The T-LI values ranged from 0.18 to 20.1% (median value 5.65%); the PCNA indices ranged from 0 to 14.7% (median value 2.45%).

The proliferation values obtained by the two methods were unrelated, as shown by a negative result of the linear correlation test.

No statistically significant difference emerged from the comparative analysis of LI values with histotype, differentiation grade and TNS parameters.

For determination of the prognostic significance of T-LI and PCNA-LI, the patients were divided into two groups.

For T-LI a discriminant value of 7.5% (above the median) was found. Thus, the difference in the two curves was statistically significant with $\chi^2 = 8.96$ ($P < 0.01$) (Figure 1). In fact, there is no biological rationale that justifies the arbitrary use of the median value as a discriminator. Various authors have shown that cell kinetics is useful only with high values, and have therefore used cut-off values above the median to analyse their data [1-4].

For PCNA in our study, neither the median value nor any other value showed any discrimination as regards survival. We, therefore, analysed survival curves only with the median value. The differences was not statistically significant ($\chi^2 = 0.38$; $P = \text{n.s.}$).

On the basis of the data reported in this study, as in our previous studies on other neoplastic pathologies (5,6,7), we conclude that T-LI analysis, whose application has already achieved the gold standard, is the most effective method for evaluation of the S phase and therefore for the prognosis for NSCLC. However, its significance in this tumour group depends on the choice of a suitable cut-off, above the median value.

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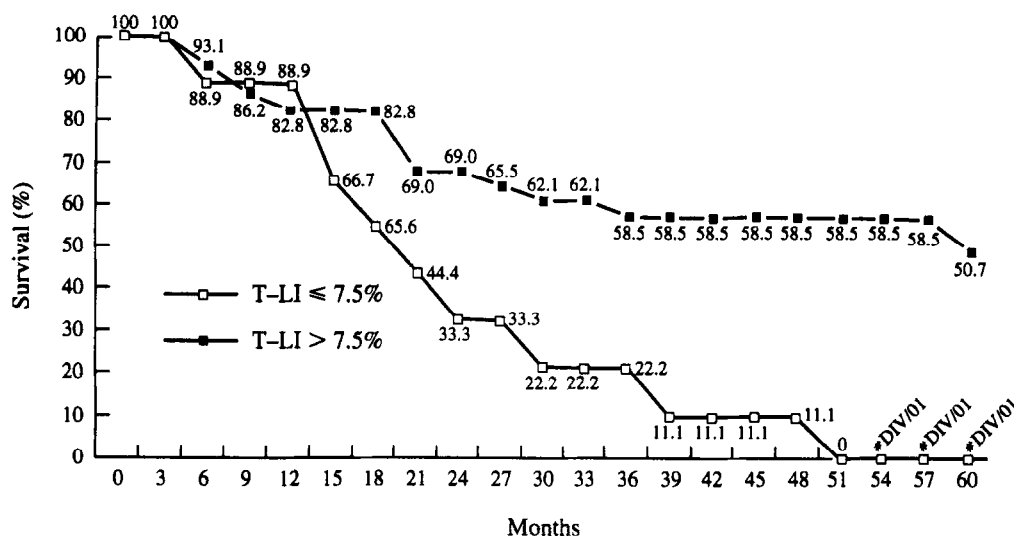


Figure 1. Survival curves according to T-LI

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Sialyl-Tn Expression in Gastric Carcinoma

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In a recent article Ma and colleagues [1] reported the results of an immunohistochemical study of the expression of sialyl-Tn in 85 gastric carcinomas. Sialyl-Tn expression occurred in 62.4% of the cases and immunoreactivity was correlated with the degree of gastric wall penetration, lymph vessel invasion, lymph node metastases, stage of the tumours and survival of the patients.

In a previous work [2], we reported the results of the immunohistochemical expression of simple mucin-type carbohydrate antigens in a series of 87 gastric carcinomas. We have used the same antibody for the detection of sialyl-Tn (TKH2), but our results do not entirely fit with those of Ma [1]. In our series, sialyl-Tn was expressed in 62/87 (71.3%) primary gastric carci-

nomas and no significant correlation was found with the different pathological parameters studied by Ma's group [1], despite the trend towards an association between sialyl-Tn positivity and signs of aggressiveness (serosal invasion, lymph node metastases and venous invasion) [2]. Our results were confirmed in a more recent study [3], using another antibody for sialyl-Tn (HB-STn, Dako, Glostrup, Denmark). In this study [3], mainly examining the expression of simple mucin-type carbohydrate antigens in precursor lesions of gastric carcinoma, sialyl-Tn was found in 75/100 (75.0%) primary carcinomas (data not previously published). Again, no significant association was found with the pathological parameters studied by Ma and colleagues [1]. However, separating the positive cases into three groups ($\leq 5\%$, $5-50\%$, $\geq 50\%$ of immunoreactive cells), we found a trend towards an association between high percentage of immunoreactive cells and aggressiveness of the tumours (serosal invasion, lymph node metastases and vascular invasion) (Table 1). These results are in keeping with those of Ma's study [1], and favour a relationship between the expression of sialyl-Tn and signs of aggressiveness in gastric carcinoma.

The aforementioned relationship was recently confirmed by Takahashi and colleagues [4] who, in a series of 350 gastric carcinomas, showed that the pre-operative serum levels of sialyl-Tn were significantly associated with signs of aggressiveness and survival of the patients. Since multivariate analysis was not performed by Takahashi's group [4], it cannot be excluded that the poor prognosis of the patients with high serum levels of sialyl-Tn was due to the significantly larger size and more advanced stage of the tumours in this group of patients.

Two other points deserve a special mention if one intends to use sialyl-Tn immunoreactivity as an independent prognostic factor.

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