



The Effect of Interaction Between Lymph Node Ratio and pN Stage

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TO THE EDITORS

We read with great interest the report by Kitamura and colleagues on the investigation of the lymph node ratio (LNR), which was defined as the ratio of metastatic lymph nodes (LNs).¹ This study suggested that a decreased LNR was associated with a detrimental effect on overall survival, especially for patients with pN1 status. We congratulate Dr. Kitamura and colleagues for this innovative and excellent study; however, two points warrant discussion.

Based on the statistical significance of LNR by Cox regression analysis, the author concluded that LNR was a more powerful risk factors that influenced survival compared with pN stage. Theoretically, pN stage, as the numerator of the ratio, was highly positively correlated with LNR. Therefore, there is considerable effect of interaction between pN stage and LNR. The interaction may explain that pN stage lost its significant correlation with survival when the two risk factors were included in the multivariate analysis.² Further analysis for effect of interaction between LNR and pN by testing an interaction term between LNR and pN stage should be carried out within the context of the multivariate Cox regression model.

Although the LNR was demonstrated to be an independent predictor by Cox regression model analysis, it is insufficient to conclude that LNR is more useful than

traditional N staging for predicting survival outcome. The strength of a predictor is related to not only the association between the predictor and the survival outcome (discriminatory) but also the distribution of the predictor in the development data (monotonicity and homogeneity).^{3,4} Thus, the author should evaluate the monotonicity and homogeneity ability of the LNR in the same cohort.

DISCLOSURES Li-Guo Wang and Jing-wen Hou declare no conflicts of interest.

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