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Refining TNM staging system for Epstein-Barr virus-related nasopharyngeal carcinoma: A multicenter cohort study

W-Z. Li[1], Y-Q. Xiang[1], H-J. Hu[2], S-H. Lv[1], G-Y. Liu[1], H. Liang[1], W-X. Xia[1]

[1] Department of Nasopharyngeal Carcinoma, Sun Yat-sen University Cancer Center, Guangzhou, China[2] Department of Radiation Oncology, The First People's Hospital of Foshan, Foshan, China

Background

Additional nonanatomic prognostic factors beyond TNM categories supplement evidence-based TNM classifications. We aimed to refine TNM staging groups for Epstein-Barr virus (EBV)-related nasopharyngeal carcinoma (NPC) by incorporating the EBV DNA status.

Methods

This multicenter retrospective cohort comprised 2,354 patients with nonmetastatic NPC treated with radiotherapy with or without chemotherapy between January 2008 and December 2016. Progression-free survival (PFS) and overall survival (OS) according to EBV DNA status and the 8th edition TNM staging system were compared. Recursive partitioning analysis (RPA) combined with supervised clustering was applied to derive prognostic groupings. A refined RPA stage was developed, validated, and compared with existing staging schemes.

Results

Pretreatment EBV DNA status was an independent prognostic factor. Lower survival probability by higher TNM stage was evident in EBV DNA (+) patients but not in those with EBV DNA (-) disease. Integrating EBV DNA status and TNM stage, the RPA stage divided nonmetastatic NPC into RPA-I (T1-3N0 or EBV DNA [-] T1-3N1), RPA-II (EBV DNA [+] T1-3N1-2 or EBV DNA [-] T1-3N2-3/T4N0-3), and RPA-III (EBV DNA [+] T4N0-3/T1-3N3) with distinctly different prognosis. The RPA stage outperformed the current TNM stage and two reported RPA staging schemes. These results were internally and externally validated. The new staging system identified approximately two-fold low-risk patients that might not benefit from chemotherapy than the current TNM staging system.

Conclusions

We developed and validated an RPA-based staging system for EBV-related NPC. This staging system may facilitate prognostic stratification and clinical trial designs.

Legal entity responsible for the study

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Disclosure

All authors have declared no conflicts of interest.