Medical Xpress

Researchers propose new staging for HPV-related oropharyngeal cancer

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Human papillomavirus (HPV) status is a strong predictor of prognosis for patients with oropharyngeal carcinoma (OPC), but the current staging system does not adequately account for biological and clinical differences between HPV-positive OPC and HPV-negative OPC, commonly caused by alcohol and tobacco use. With rates of HPV-related OPC rising rapidly, researchers at The University of Texas MD Anderson Cancer Center propose a new staging system to more accurately predict patient outcomes and identify the most appropriate treatments.

In a study published in the current issue of the *Journal of Clinical Oncology*, MD Anderson researchers explored alternative staging criteria based on the current TNM Staging System, the world's most commonly used classification tool to stage different types of cancers. The TNM Staging System is based on the tumor (T category), whether or not the cancer has reached nearby lymph nodes (N category), and metastasis (M category). According to accepted theories, there are four characteristics of useful stage groupings:

- similar survival rates for patients within groups defined by "T" and "N" categories;
- significantly different survival rates across groups;
- accurate prediction of outcome; and
- balanced distribution of patients between groups.

Using data from more than 660 patients treated at MD Anderson

between January 2003 and December 2012, the researchers showed that applying the current TNM staging criteria to patients with HPV-positive OPC did not meet these criteria. They did not find differences in survival between stage groups, and the distribution of patients was unbalanced, with the majority of patients classified as having stage IV disease by the current criteria. Thus, they sought to develop a revised staging system that would separate patients with HPV-related OPC.

"Staging is a critical component of designing treatment plans and for predicting and helping patients understand their prognosis," said corresponding author, Erich M. Sturgis, M.D., professor in the Department of Head and Neck Surgery. "Patients with HPV-positive OPC tend to present with more advanced disease, but also typically have better survival rates than those with HPV-unrelated OPC. These cancers are markedly different and require different staging criteria."

In the last few decades, the number of HPV-related OPC cases - cancers of the middle part of the throat, including the base of the tongue, the tonsils, the soft palate, and the walls of the pharynx - have increased drastically. Based on data from U.S. cancer registries, an estimated 72 percent of OPCs each year - over 11,000 cases - are associated with prior HPV infection. HPV-related OPCs are up to five times as common in men as in women and, though non-HPV OPCs are typically diagnosed in older populations, HPV-related OPCs tend to affect patients in their 40s and 50s, according to the American Cancer Society.

As they explored different stage groupings to predict survival in this patient population, the researchers found that the "T" category was most important and that the "N" category appeared to have no predictive effect - until they replaced OPC "N" with the "N" category from another cancer of the throat related to a different virus, nasopharyngeal carcinoma (NPC; cancer of the upper part of the throat, behind the nose). "T" category was still the most important, but the "N" category

became a significant predictor of survival among patients who had HPV-positive OPC. This is the first time that NPC "N" categories have been applied to HPV-positive OPC.

Thus, the MD Anderson researchers developed new stage groupings with both traditional OPC "T" categories and the NPC "N" categories:

- Division of patients with stage I disease into two groups: stage IA, defined as T1, N0-N2; and stage IB, defined as T2, N0-N2;
- Stage II would be defined as T1-T2, N3 or T3, N0-N3;
- Stage III would be defined as T4 regardless of nodal involvement; and
- Stage IV would be all M1 tumors.

These new groupings were proven to better separate patients with HPV-positive OPC with respect to survival than does the current TNM staging system for OPC. Further, with these new stage groupings, the risk of death increased with each stage and patients with stage III disease had five times the risk of death versus patients with stage IA disease - illustrating that the new groupings better meet the useful staging criteria.

"The revised staging system has greater predictive power than the current system, which has been shown to be insufficient for HPV-positive OPC," said Sturgis. "Although confirmation of our findings in patients at other institutions is needed, we believe that NPC "N" categories should be strongly considered as an alternative to the traditional OPC "N" categories as the TNM staging system evolves."

Provided by University of Texas M. D. Anderson Cancer Center

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