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Editorial

Survival Trends in Head and Neck Cancer: Opportunities for Improving Outcomes

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Cancer registry and population-based data are valuable sources of information on the incidence, survival, stage at diagnosis, and demographic distribution of specific malignancies. They can be a reflection of prior and current public health programs, advancements in diagnosis and cancer therapy, and health care availability. In the current economic climate, in which health care reform and allocation of limited resources are administrative priorities, the report by Pulte and Brenner in this issue [1] raises critical issues about improving outcomes and further scientific inquiry in this disease.

Squamous cell cancer of the head and neck has historically been viewed as a disease related to a lifestyle involving heavy tobacco and alcohol exposure. It is a disease often curable at diagnosis, but is associated with poor survival as a result of patient comorbidity, second malignancies of the aerodigestive tract, and social factors that impact the success of treatment, including poor compliance, restricted access to health care, and limited patient resources. Public health efforts at curbing tobacco consumption that began in the 1950s have been successful in decreasing the incidence of other tobacco-related malignancies such as lung cancer and squamous cell cancers of the esophagus. However, a similar decline in cancer incidence has not been observed for head and neck cancers.

The authors conducted a review of Surveillance Epidemiology and End Results data for 1973–2006 and observed that, although the overall incidence of head and neck cancer in that time period was stable, there was a significant improvement in overall survival, most notably in those patients with tongue and tonsil cancer, and particularly over the past decade. Although this kind of analysis can be subject to a number of flaws, especially in primary site and stage assignment, the increase in survival is undeniable and impressive.

Obvious explanations come to mind, including improvements in staging (with the resulting "Will Rogers" effect), and improvements in treatment. The negative impact of continued tobacco use on treatment outcome has been well recognized [2–4], and therefore the decrease in tobacco use in recent years may also be contributing to this improvement in survival. However, the more compelling explanation is the change in the natural history of this disease most apparent in the last decade [5–9]. Several retrospective and prospective, U.S. and European studies over the last 5–10 years have demonstrated an epidemiologic

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shift in this disease, with a dramatic increase in the frequency of human papillomavirus (HPV)-related oropharynx malignancies.

HPV-related oropharynx (tonsil and base of tongue) cancers appear to have a predilection for younger white men, and appear to be molecularly distinct from tobacco-related head and neck cancers [5–9]. This unique subset of cancers is associated with less tobacco and alcohol exposure, less cardiopulmonary comorbidity, and, most importantly, a superior prognosis than with tobacco-related head and neck cancers.

Compelling data that the prognostic value of HPV may be modified by other risk factors or environmental exposures have also now surfaced. Ang et al. [10] recently reported the impact of tobacco exposure on the treatment outcome of HPV-related oropharynx cancers treated with concurrent chemoradiation in a retrospective analysis of the large Radiation Therapy Oncology Group 0129 clinical trial. Among patients with oropharyngeal cancer treated in that study, recursive partitioning allowed the definition of low-, intermediate-, and high-risk patients based on HPV status, smoking history, as well as tumor and node descriptors. HPV^+ nonsmokers or very light smokers represent the low-risk individuals whereas HPV^- smokers are at high risk for death from this disease.

Cancer registry data and population-based observations give little insight into the impact of cancer treatment on quality of life issues. At present, because of a lack of clinical data to support otherwise, HPV-related oropharyngeal cancer is approached with the same treatment strategies as HPV− cancers of the head and neck. Locally advanced disease, the most common stage at presentation, often involves curative intent multimodality therapy consisting of chemotherapy and radiation, with or without surgery. It is well recognized that the better survival outcomes from contemporary treatment regimens come at the cost of significant debilitating late toxicity in a proportion of patients.

The ability to separate subsets of head and neck cancer patients with a better prognosis suggests that a risk-based treatment approach may be applicable in squamous cell cancers of the head and neck. It seems logical to study HPV^+ oropharynx tumors separately in contemporary prospective clinical investigation, or at the very least stratify according to HPV status. Certainly, limiting toxicity and improving quality of life outcomes without compromising treatment efficacy should be priorities in the lowest risk subset, whereas improving survival should remain the priority in those with intermediate- or high-risk disease.

This change in disease etiology also provides an opportunity to impact its incidence through cancer prevention strategies. The great majority of HPV-related head and neck cancers have been found to harbor the HPV 16 subtype. Two U.S. Food and Drug Administration approved vaccines—Cervarix® (GlaxoSmithKline, Middlesex, UK) and Gardasil® (Merck, Whitehouse Station, NJ)—confer immunity against HPV-16 and have been shown, in large phase III clinical trials, to be highly efficacious in preventing persistent high-risk HPV infections and subsequent premalignant anogenital lesions when administered prior to onset of sexual activity [11–13]. The impact of vaccination on the incidence HPV-related malignancies in both men and women will be contingent on the implementation of an affordable, accessible, universal, and gender-neutral vaccination program prior to sexual activity. In 2009, the Centers for Disease Control revised their recommendations for routine preteen vaccination against HPV to include males; however, implementation of these recommendations has lagged behind.

Despite this marked change in epidemiology, and the improvement in survival documented by these authors, head and neck cancer remains a difficult disease that is linked to exposure to identifiable carcinogens, particularly tobacco. The need to improve both treatment and quality of life outcomes in this challenging group of patients is apparent, and is the focus of continued clinical investigation. Public health policy focused on eliminating continued tobacco use and improving access to health care in this often indigent and minority population should be prioritized.

Author Contributions

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