Is AJCC/UICC Staging Still Appropriate for Head and Neck Cancers in Developing Countries?

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Abstract
By 2030, 70% of cancers will occur in developing countries. Head and neck cancers are primarily a developing world disease. While anatomical location and the extent of cancers are central to defining prognosis and staging, the American Joint Committee on Cancer (AJCC)/International Union Against Cancer (UICC) have incorporated non-anatomical factors that correlate with prognosis into staging (eg, p16 status of oropharyngeal cancers). However, 16 of 17 head and neck surgeons from 13 African countries cannot routinely test for p16 status and hence can no longer apply AJCC/UICC staging to oropharyngeal cancer. While the AJCC/UICC should continue to refine staging that best reflects treatment outcomes and prognosis by incorporating new non-anatomical factors, they should also retain and refine anatomically based staging to serve the needs of clinicians and their patients in resource-constrained settings. Not to do so would diminish their global relevance and in so doing also disadvantage most of the world’s cancer patients.

Keywords
cancer, staging, UICC/AJCC, developing countries, head and neck, p16, oropharyngeal

Commentary
The American Joint Committee on Cancer (AJCC) Cancer Staging Manual is jointly developed by the AJCC and the International Union Against Cancer (UICC).1 In the seventh edition of the manual, it is stated that,

Classification and staging of cancer enable the physician and cancer registrar to stratify patients, which leads to better treatment decisions and the development of a common language that aids in the creation of clinical trials for the future testing of cancer treatment strategies. A common language of cancer staging is mandatory to realize the important contributions from many institutions throughout the world.

Most cancers occur in developing countries, and developing countries are projected to account for 70% of cancers by 2030.2 Developing countries also account for 67% of head and neck cancers and 82% of head and neck cancer–related deaths.3 Cancer of the head and neck is therefore primarily a disease of the developing world. However, the way head and neck cancers are investigated and treated in developed versus developing countries is increasingly divergent because of technological advances and financial and infrastructural differences. Thus, having a staging system that is globally applicable is becoming ever more difficult to achieve.
While anatomical location and extent of disease have been and remain central to defining cancer prognosis and hence staging, an increasing number of nonanatomic factors that correlate with prognosis are (quite appropriately) being incorporated into stage groupings. An example is the incorporation of p16 status in staging of oropharyngeal carcinoma in the eighth edition of the AJCC Cancer Staging Manual. While p16 status currently serves only as a prognostic marker, it may in the future, together with other nonanatomical tests, serve to select and stratify care. Yet, for all 16 of 17 fellowship-trained head and neck surgeons from 13 Sub-Saharan African countries who coauthored this commentary (Figure 1), p16 testing is not routinely available for their patients with oropharyngeal cancer because of the lack of laboratory facilities in their countries and/or unaffordability of the test. Because the new AJCC/UICC staging system for oropharyngeal cancer does not include a category for “p16 not available,” the new staging therefore cannot be applied to oropharyngeal cancer patients in many (if not most) developing countries.

Another challenge that staging bodies must consider is the diversity of the type and quality of therapeutic interventions in developed versus developing countries that might affect outcomes and prognosis. Only 24 of 52 African countries have radiotherapy facilities, and treatment delays may be up to 46 weeks. Likewise, certain chemotherapy drugs and most targeted agents are not available to patients in these countries. Such diversity in management might invalidate the current favorable prognosis for advanced p16+ oropharyngeal cancer in the current staging in such resource-constrained settings.

A further concern is that having staging systems incorporating nonanatomical factors that are not available in middle- and lower-income countries could potentially discourage “the creation of clinical trials for the future testing of cancer treatment strategies” and other clinical research as it becomes more difficult to publish such clinical research (eg, on oropharyngeal cancer without including the p16 status of patients).

How then do we address this challenge of creating a globally applicable staging system? While the authors would encourage the AJCC/UICC to continue to refine staging systems that best reflect treatment outcomes and prognosis by incorporating new nonanatomical factors, we would encourage them also to retain and continue to refine anatomically based staging systems to serve the needs of clinicians and their patients in resource-constrained settings who by 2030 will account for 70% of the global cancer burden.

A model that may be applied is that of a staging system that considers available diagnostic and therapeutic resources, as has been done in the African Head and Neck Society Clinical Treatment Guidelines for Head and Neck Cancer. In this web-based treatment guideline, clinicians are directed to treatment protocols that are precisely tailored to the diagnostic and therapeutic resources available to the clinician and to the patient (https://afhns.org/head-neck-cancer-guidelines/).

If the AJCC and UICC were to not take up this challenge of developing resource-appropriate staging, it would reduce their global relevance and in so doing also disadvantage most of the world’s cancer patients.

**Figure 1.** Thirteen countries (red) with 586m inhabitants represented in the survey.

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References

1. American Joint Committee on Cancer. *American Joint Committee on Cancer (AJCC) Cancer Staging Manual*. 7th edition. Accessed February 8, 2020. https://cancerstaging.org/references-tools/descriptions/Documents/AJCC%207th%20Ed%20Cancer%20Staging%20Manual.pdf

2. Farmer P, Frenk J, Knaul FM, et al. Expansion of cancer care and control in countries of low and middle income: a call to action. *Lancet*. 2010;2;376(9747):1186-1193.

3. Patterson RH, Fischman VG, Wasserman I, et al. Global burden of head and neck cancer: economic consequences, health, and the role of surgery. *Otolaryngol Head Neck Surg*. 2020;194599819897265. doi:10.1177/0194599819897265

4. Fagan JJ, Zafereo M, Aswani J, Netterville JL, Koch W. Head and neck surgical subspecialty training in Africa: sustainable models to improve cancer care in developing countries. *Head Neck*. 2017;39(3):605-611

5. AfHNS Clinical Practice Guidelines for Head & Neck Cancers in Developing Countries and Limited Resource Settings. February 10, 2020. https://afhns.org/head-neck-cancer-guidelines/