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Letter to the Editor

Staging of Differentiated Thyroid Carcinoma: Standardizing Rational Thought

In the current edition of the Journal, Lang et al.[1] studied a population of 760 patients with well-differentiated thyroid cancer who were retrospectively restaged on the basis of the updated criteria of the 6th edition of the *AJCC Cancer Staging Manual*.[1,2] In the updated staging system, the designation of a T1 tumor has been increased from ≤ 1 cm to ≤ 2 cm; T2 tumors are now > 2 cm and ≤ 4 cm; T3 tumors now include those with minimal extrathyroidal extension; and T4 tumors have been subcategorized into T4a (invading subcutaneous tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve) and T4b (invading prevertebral fascia or encasing carotid artery or mediastinal vessels). These changes more than doubled the percentage of T1 tumors, with a reciprocal diminution in T2 tumors. The frequency of T3 tumors increased from 10% to 33.7%, and the frequency of T4 tumors decreased from 31.6% to 7.9%.[1]

Nodal metastases have also been recategorized from the previous N1a, which included both central and ipsilateral cervical metastases, to the newer edition of N1a, which is limited to the central neck (level VI nodes). Because of this more restrictive definition, the frequency of patients with N1a disease decreased in the Lang series from 25.7% to 4.7%, with a reciprocal increase in N1b disease.[1] The staging categories have also been changed and expanded from a single category of stage IV to encompass four new subcategories.

Overall, the Lang data suggest that the 6th edition has better clinical use compared with the 5th edition, and therefore, when comparing patient populations, it seems to have better disease predictability. The data are carefully analyzed, and the author's conclusions are well founded. But the article needs to be viewed in a broader context.

Well-differentiated thyroid cancer is a relatively indolent malignancy characterized by a high recurrence rate but a relatively low cancer-specific mortality rate. Treatment consists of surgery, radioactive iodine ablation, and long-term suppression of the pituitary secretion of TSH by exogenous administration of thyroid hormone. Occasionally, other therapeutic interventions, including external-beam radiotherapy and a variety of chemotherapy protocols, are used for unresectable, unresponsive, or metastatic disease.

Clinicians have looked to evidence-based guidelines to tailor individual patient treatment. These guidelines have been based on large cohorts of previously treated patients with well-characterized treatment- and tumor-related morbidity. Accordingly, the value of a tumor staging system is appreciated and embraced by virtually everyone involved in oncologic care. Unfortunately, well-differentiated thyroid cancer is plagued by the presence of multiple staging systems, each of which has its proponents and detractors. The plethora of staging systems is cumbersome and confusing, particularly to our ever-sophisticated patient population. In addition to endorsement of the tumor, node, metastasis (TNM) staging system, there are proponents for other staging systems, including AMES (age, metastasis to distant sites, extrathyroidal invasion, size), AGES (age, tumor grade, extent, size), and MACIS (metastases, age, completeness of resection, invasion, size).[3] The net effect creates more ambiguity than clarity. The TNM staging system, as reported by the American Joint Committee on Cancer (AJCC), represents the collaborative work of virtually every major cancer society, including the International Union Against Cancer (UICC). This system reflects a dynamic process endorsed by the editors, notably Frederick L. Green, MD, and the editor of this journal, Charles M. Balch, MD, who had the foresight to note that "staging is not a fixed science."[5] For a system to be useful, it needs to be periodically updated to account for new information about both diagnostic procedures and treatment protocols. A formal protocol has been implemented for continuous improvement of the TNM classification on the basis of clinical relevance, prognostic evidence, and acceptance by the members of the UICC commit-

tee.[5] The changes in the AJCC staging system for thyroid cancer typify this process and are likely to improve their use in the clinical setting. It is therefore essential that individuals engaged in patient care adopt the AJCC TNM as the standard system to report every patient with thyroid malignancies.

Despite the benefits of evidence-based updates of a staging system, there are potential negative implications. Each time a staging system is upgraded, stage migration will likely occur. Therefore, reliance on previous well-conducted trials becomes ever more problematic and limits the use of such studies when comparing patient outcomes. This unfortunate, but requisite, limitation emphasizes the importance of prospective randomized trials to mitigate against these limitations. Because of the indolent nature of well-differentiated thyroid cancer, we will not know the effects of these modifications for decades. Nonetheless, the study in this issue by Lang et al., as well as additional recent publications, will help shed light on these issues.[1,6,7] It is also certain that newer diagnostic and therapeutic options will be developed and that subsequent classification changes will be required. Despite these limitations, the thyroid cancer community should accept the 6th edition of the *AJCC Cancer Staging Manual* and use it as its primary mode for staging thyroid malignancies.

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