Clinical THYROIDOLOGY



The AJCC TNM Staging Underestimates **Risk in Young Patients with More Aggressive Differentiated Thyroid Cancer**

Tran Cao HS, Johnston LE, Chang DC, Bouvet M. A critical analysis of the American Joint Committee on Cancer (AJCC) staging system for differentiated thyroid carcinoma in young patients on the basis of the Surveillance, Epidemiology, and End Results (SEER) registry. Surgery. April 11, 2012 [Epub ahead of print].

SUMMARY • • • • • • •

Background

The differentiated thyroid cancer (DTC) staging system of the American Joint Committee on Cancer (AJCC) uses age for staging the patient. Patients less than age 45 with distant metastases are stage II, while patients age 45 or older with metastases are stage IV. Although age is linked to prognosis, it may be too optimistic to classify younger patients in this way. This study examined the effect of age and disease extent in the AJCC staging system on mortality using survival data from the Surveillance, Epidemiology, and End Results (SEER) Program from 1973 to 2005 in order to determine whether the risk stratification accurately portrayed outcomes of DTC for young patients.

Methods

The SEER data set includes data on the primary tumor, demography, spread, histology, and mortality across multiple geographic regions. The examiners included patients with DTC as their only malignancy between 1973 and 2005. They used Cox multivariate proportional-hazards models to generate a relative risk of death by any cause with 95% confidence intervals, controlling for sex, race, marital status, histology, surgical and radiation treatment, age at diagnosis, and stage.

Results

The SEER database had sufficient data to generate the tumor-node-metastasis (TNM) stage using the AJCC Cancer Staging Manual, 6th edition for 49,240 patients. The mean (±SD) age was 44.6±15.5 years. In the multivariate analysis, increasing age correlated with increased mortality. There was an approximately 50% increased mortality for every decade from age 40 to age 90. The magnitude of the age effect was greater in women than in men.

In patients less than age 45, the mortality of stage II was 11-fold greater than that of stage I, but in those age 45 or older there was no significant increase in risk between stages I and II. Survival of patients less than 45 years old with stage II was worse than older stage II patients who had tumors of 2 to 4 cm confined to the thyroid gland. When the TNM staging for age 45 or older was applied to those less than age 45, there was an increase of mortality hazard ratio for those now reclassified as stage III or IV based on lymphnode involvement and tumor spread outside the thyroid but without distant metastases.

Conclusions

The presence of regional spread and distant metastatic DTC bears prognostic significance for all ages. Under current AJCC guidelines, young patients with metastatic thyroid cancer may be understaged.

ANALYSIS AND COMMENTARY • • • • •

There are many different staging systems for thyroid cancer (1, 2), but in recent years there has been increasing acceptance of the AJCC TNM system as the most convenient and widely applicable for DTC. This excellent paper confirms the adverse effect of increasing age on mortality in patients with DTC. Another recent paper reported increased cause-specific mortality in Japanese patients over age 60 who had papillary thyroid cancer (3). However, the TNM staging system's emphasis on age, as the current paper points out, underestimates mortality in young patients. This continued on next page

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The AJCC TNM Staging Underestimates Risk in Young Patients with More Aggressive Differentiated Thyroid Cancer

underestimate is widely known by practitioners who use more aggressive therapy in young patients with extrathyroidal spread, especially those with distant metastases. Although older work emphasized the lack of effect of spread to lymph nodes on mortality in young patients (4), other analyses concluded that positive lymph nodes were associated with more frequent recurrences (5). The current study demonstrated a significant adverse effect of nodal disease on survival in both age groups.

It should be noted that almost one-fourth of newly diagnosed DTC patients in the SEER database were between ages 40 and 50 years. This makes the age 45

threshold for staging somewhat arbitrary. Limitations of the study are that the SEER database did not contain data on specific histology or vascular invasion. The study did not analyze recurrence, a more frequent event than mortality in patients with DTC. The study did not control for the effect of treatment on survival. In fact, the paper uses the term radiation rather than specifically denoting therapy with radioiodine-131. All in all, I must agree with the authors' recommendation that the AJCC system needs to be revised, with more specific and detailed staging for young patients.

- Jerome M. Hershman, MD

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