Tumor histology is not an independent determinant of the prognosis of differentiated thyroid cancer


SUMMARY

BACKGROUND Papillary and follicular thyroid cancer are often considered together in analyses of differentiated thyroid cancer; however, follicular cancer generally has a more aggressive course with less favorable survival rates. On the other hand, some studies suggest that the two tumors have inherently similar biologic behavior when adjusted for patient age, tumor stage and initial therapy. The aim of this study was to investigate whether there are differences in tumor-specific survival when adjusted for initial staging.

METHODS This is a retrospective study of papillary thyroid cancer (PTC) and follicular thyroid cancer (FTC) that was treated at the University of Würzburg from January 1978 through December 2002. The 2002 cutoff was selected to ensure a minimum follow-up of 5 years. All patients were treated with total thyroidectomy and \( ^{131}I \) for remnant ablation except for patients with isolated papillary thyroid microcarcinoma (tumors ≤1 cm). Patients were usually treated with 40 to 95 mCi (1500 to 3500 MBq) of \( ^{131}I \) according to the thyroid remnant size. Patients had follow-up 6 to 12 months after the initial treatment when \( ^{131}I \) whole-body scintigraphy and thyroglobulin (Tg) measurements were performed after levothyroxine withdrawal or recombinant human thyrotropin (rhTSH) stimulation. Persistent or recurrent disease was treated with 190 mCi (7000 MBq) of \( ^{131}I \). Within the first 5 years after initial therapy, patients who were considered to be free of disease had one more whole-body diagnostic scans and serum Tg measurements after thyroid-hormone withdrawal or rhTSH stimulation. Thereafter, serum Tg measurements were made during thyroid-hormone suppression of TSH and neck ultrasonography, and computed tomography scans or magnetic resonance imaging was performed as indicated. Tumor staging was done according to the World Health Organization standard at the time of surgery. Tumor size was measured on the primary tumor specimen. Patients had to undergo lymph-node surgery to be considered free of lymph-node metastases.

RESULTS The study subjects were 875 patients with PTC (71%), and 350 with FTC (29%). There were 628 (72%) women with PTC and 228 (65%) with FTC; the mean age was 46.1 years (range, 5 to 87) in the PTC patients and 52.2 years (range, 8 to 81) in the FTC patients (P<0.001, comparing PTC with FTC) (Figure 1). Mean follow-up was 10.8 years in the PTC group and 10.9 years in the FTC group. Mean (±SD) tumor diameter in PTC and FTC was 19.2±0.6 and 31.7±1.3 mm, respectively (P<0.001). Tumor was multifocal in 92 (10.5%) and 51 (14.5%) (P = 0.047), metastatic to lymph nodes in 78 (8.9%) and 18 (5.1%) (P = 0.02), and metastatic to distant sites in 64 (7.3%) and 55 (15.7%) (P<0.001) in the two histologic tumor types, PTC and FTC, respectively. The median follow-up for the entire cohort was 9.9 years, without a significant difference in the length of follow-up in the two groups of patients. Tumor-specific mortality of PTC and FTC were considerably different: the 20-year survival rates were 90.6% for PTC and 73.7% for FTC (P<0.001). If distant metastases were excluded from the analysis, the 20-year disease-specific mortality rates in FTC patients was 80.2%, which was significantly lower than that for PTC (93.1%) (P<0.001). Moreover, in patients with distant metastases, there were no significant difference between PTC and FTC (P = 0.16). In Cox regression, the independent
variables for survival were the presence of distant metastases (P<0.001), age (P<0.001), tumor size (P = 0.001), and extrathyroidal invasion (P = 0.007) at the time of diagnosis. In addition, Kaplan–Meier curves did not show significant differences between PTC and FTC for patients younger than 45 years of age with isolated nonmetastatic tumors <1 cm (P = 0.81).

CONCLUSION The independent risk factors for tumor-specific survival were distant metastases, patient age, tumor size, and extrathyroidal invasion, but not tumor histology.

Verburg et al. suggest that there are several sources of concern in their study. They were unable to confirm some of the data because in the earlier part of the study, pathology reports were rather scarce. Also, a large number of patients did not have information on the presence or absence of lymph-node metastases; and over time, there may have been shifts in tumor treatment. The authors also acknowledge that it is still not clear why patients with follicular cancer present with more advanced disease than patients with papillary thyroid cancer.

Nonetheless, it is important to know that features such as patient age, tumor stage, and initial treatment have a major impact on the clinical outcome of both papillary and follicular cancer, which to some extent puts less emphasis on tumor histology alone when attempting to estimate the risks of tumor recurrence and cancer-specific mortality.

Verburg FA, et. al.

Ernest L. Mazzaferri, MD MACP

References