THE DOUBLING TIME OF SERUM THYROGLOBULIN IS A VERY STRONG PREDICTOR OF PROGNOSIS IN PATIENTS WITH PAPILLARY THYROID CARCINOMA



Miyauchi A, Kudo T, Miya A, Kobayashi K, Ito Y, Takamura Y, Higashiyama T, Fukushima M, Kihara M, Inoue H, Tomoda C, Yabuta T, Masuoka H. **Prognostic impact of serum thyroglobulin doubling-time under thyrotropin suppression in patients with papillary thyroid carcinoma who underwent total thyroidectomy.** Thyroid 2011;21:707-16. Epub June 7, 2011.

BACKGROUND

Measureable thyroglobulin (Tg) levels in patients with papillary thyroid carcinoma after initial therapy are suggestive of persistent or recurrent disease. The purpose of this study was to examine the serum Tg kinetics in patients with papillary thyroid carcinoma and to correlate the Tg doubling time (Tg-DT) with the prognosis.

METHODS AND RESULTS

From January 1998 through December 2004, a total of 426 patients had a total thyroidectomy for papillary thyroid carcinoma and had at least four measurements of Tg with negative Tg antibody and a suppressed thyrotropin level (<0.1 mIU/L). This group of patients was composed of 349 women and 77 men, between 14 and 81 years of age (mean, 51.5). The tumor status in tumor-node-metastasis (TMN) staging was T1 (in 43 patients), T2 (in 129), T3 (in 119), and T4 (in 135). Radioiodine was given to 167 patients. In this retrospective study, the Tg-DT was calculated based on Tg tests obtained during routine follow-up. For the majority of the patients, Tg levels were measured 1 and 3 months after surgery and two times per year thereafter. The Tg measurements were more frequent in the high-risk patients and once a year in the very-low-risk patients. Neck sonography was performed annually with chest x-ray examination or computed tomography scanning, if indicated. Patients were followed for a mean of 88.1 months and a median of 86.7 months. During the study period, 6 patients died of the disease, 58 had locoregional recurrences, and 25 had distant metastases. A total of 137 of the 426 patients had detectable Tg levels. Patients were placed into four groups based on their calculated Tg-DT of <1 year (17 patients), 1 to 3 years (21), \geq 3 years (30), and a negative Tg-DT due to decreasing Tg levels (69). A total of 88 patients were excluded from analysis because they had fewer than four Tg measurements and 201 had Tg levels that were always below the level of detection. The causespecific survival correlated with the Tg-DT. Fast Tg-DT (<1 year) had a 10-year cause-specific survival of 50%, while a Tg-DT of 1 to 3 years had 95% survival. Groups with a Tg-DT of >3 years, a Tg-DT with a negative slope (Tg level decreasing with time), or a Tg level always lower than the detection limit had a cause-specific 10-year survival of 100%. The Tg-DT calculated using only the first four data points or all data points was the only independent predictor of survival, distant metastases, and locoregional recurrence on multivariate analysis.

CONCLUSION

Tg-DT is a very strong predictor of prognosis in patients with papillary thyroid carcinoma.

Other investigators, including Baudin et al. (1), have noted that a rising Tg was associated with detection of recurrent disease while a stable or falling Tg, especially if <10 ng/ml, was an indication of quiescent disease with a low positive predictive value of detecting recurrence. Similarly, serum calcitonin doubling time is a strong prognostic factor for recurrence and death from medullary thyroid carcinoma (2). This study demonstrates that the Tg-DT can be determined by the first four measurements, and the shorter time is associated with lower cause-specific survival and increased risk for distant metastases and locoregional recurrence. The Tg-DT derived from

continued on next page

Miyauchi A, et al.

predicting the risk of death. This investigation has put a quantitative number on what we are already knew clinically, namely that patients with rising Tg levels are at high risk for recurrence and death. We should use the Tg-DT in the same way we use calcitonin doubling time to predict which patients with medullary thyroid cancer are at high risk for recurrence and death.

- Stephanie L. Lee, MD, PhD

References

1. Baudin E, Do Cao C, Cailleux AF, Leboulleux S, Travagli JP, Schlumberger M. Positive predictive value of serum thyroglobulin levels, measured during the first year of follow-up after thyroid hormone withdrawal, in thyroid cancer patients. J Clin Endocrinol Metab 2003;88:1107-11.

the first four data points was a significant prognostic

factor in univariate and multivariate analysis. In this study, thyroid cancer–specific deaths occurred only in

stage IV disease. But only 6 of 189 (3.2%) of patients

in stage IV died of the disease, giving a 10-year cause-

specific survival rate of 94.6%. Using the Tg-DT, 5 of

17 patients with a Tg-DT of <1 year and 1 of 21 of

patients with Tg-DT of 1 to 3 years died of thyroid cancer, while none of the patients in the other groups

died. Thus, the Tg-DT was better than TMN staging at

THE DOUBLING TIME OF SERUM THYROGLOBULIN

IS A VERY STRONG PREDICTOR OF PROGNOSIS IN PATIENTS WITH PAPILLARY THYROID CARCINOMA

> 2. Miyauchi A, Onishi T, Morimoto S, Takai S, Matsuzuka F, Kuma K, Maeda M, Kumahara Y. Relation of doubling time of plasma calcitonin levels to prognosis and recurrence of medullary thyroid carcinoma. Ann Surg 1984;199:461-6.



