

## PROGNOSTIC VALUE OF THE RATIO THYROGLOBULIN TO I-131 UPTAKE AFTER THYROIDECTOMY BEFORE ABLATIVE RADIOIODINE THERAPY IN WELL-DIFFERENTIATED THYROID CANCER

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### ABSTRACT

Before I-131 treatment, serum Tg is not a reliable tumor marker since it can also be originated from remnant thyroid tissue or postsurgery trauma. We evaluated serum Tg and I-131, 24 hours uptake before the first I-131 treatment in 214 patients with well-differentiated thyroid cancer (74 papillary/140 follicular). The highest value of the ratio serum Tg to I-131, 24 hours uptake in tumor-free patients (Group A) was 12.81 ng/ml/%. Therefore the ratio higher than 12.81 ng/ml/% was indicative of metastasis or later recurrence. The sensitivity for lymph node metastases, distance metastases and late recurrence were 41.38%, 88.37%, 76.47%, respectively. The Tg/I-131 uptake ratio might be used as a prognostic value for well-differentiated thyroid cancer patients after thyroidectomy and before I-131 treatment.

Serum Thyroglobulin (Tg) is a suitable tumour marker for differentiated thyroid cancer after total thyroidectomy by surgery and I-131 ablation or treatment. In these cases serum Tg is a very reliable marker for the local recurrence of thyroid cancer, lymph node metastases and distance-site metastases. Unfortunately, immediately after surgical ablation, serum Tg can be of limited value and elevated serum Tg levels are particularly evident after incomplete thyroidectomy.<sup>1</sup> Surgical ablation could be expected to increase serum Tg by disruption of the thyroid structure. With remnant thyroid tissue, serum Tg could be expected to be originated from the normal remnant plus tumor masses. In remnant with no tumor burden, serum Tg would be low and directly correlated to the mass of the thyroid remnant. It

was hypothesized that the ratio of serum Tg to I-131 uptake could be used to correct Tg value for variations in the remnant tissue. The purpose of study was undertaken to evaluate the hypothesis that the ratio of serum Tg to I-131 24 hours uptake in the thyroid bed could be used during postsurgery conditions and before I-131 treatment to detect thyroid cancer (distance metastasis or late recurrence).

### MATERIALS AND METHODS

This study was the retrospective data of 343 well-differentiated thyroid cancer patients treated with I-131 at Division of Nuclear Medicine, Siriraj Hospital since 1990- 1997. Two hundred and fourteen patients were studied (74 papil-

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lary 140 follicular ) with Tg and I-131 24 hours uptake in thyroid bed before I-131 therapy. One hundred and twenty nine patients were excluded because positive Tg-specific auto-antibodies or Tg and I-131 uptake were not obtained pre-radioiodine treatment. The patients were evaluated in four groups by following criteria.

- Group A** = disease-free, no local recurrence or metastases.
- Group B** = lymph node metastases
- Group C** = distant metastases with or without lymph node involvement
- Group D** = late recurrence at lymph node or distance site.

**THYROGLOBULIN MEASUREMENT**

Unfortunately, Tg could not be measured using the same technique in all patient. Serum Tg measurement before 1997 was performed by RIA technique and Serum Tg measurement since 1997 was performed by IRMA technique.

**RESULTS**

**Table 1.** Data of 214 well-differentiated thyroid cancer patients

Patients	Group A	Group B	Group C	Group D
Number	96	58	43	17
Mean of age (Years)	42.75	46.72	51.60	51.63
Cell type - papillary	40	9	21	4
- follicular	56	49	22	13
Sex -male	12	23	12	5
-female	81	35	31	12

**Table 3.** Number of patients in Group A, B, C, and D which Tg/ I-131 uptake ratio more than 12.81 ng/ml/% (positive result) and less than 12.81 ng/ml/% (negative result )

Group of patients	Tg/ I-131 uptake ratio ≤12.81 ng/ml/%	Tg/ I-131 uptake ratio ≥ 12.81 ng/ml/%	total of patients
A	96	0	96
B	34	24	58
C	5	38	43
D	4	13	17

**24 HOURS I-131 UPTAKE MEASUREMENT**

Iodine-131 uptake in the thyroid bed was measured by Gamma Spectrometer with flat field collimator after 24 hours oral administration of 10 µCi I-131

**STATISTICAL ANALYSIS**

Tg/ I-131 uptake ratio were calculated for all patients. The histogram of the ratio Tg to I-131 uptake revealed non-normal distribution of the data. Initially Mann-Whitney U test was used to test four groups of patients and the results were significant differences between all groups as describe in the result (Table 2). The use of maximum Tg/ I-131 uptake ratio in patients group A is 12.81 ng/ml/% to identify high probability of metastasis or late recurrence. We used the value of Tg/ I-131 uptake ratio more than 12.81 ng/ml/% as positive results in patients groups B, C, and D.

**Table 2.** Tg/ I-131 24 hours uptake ratio (ng/ml/% ) in patients Group A, B, C, and D

	Group A	Group B	Group C	Group D
No of patients	96	58	43	17
Mean	2.5	23.7	79.5	80.3
Range	12.8	394.3	611.6	737.7
Maximum	12.81	394.33	613.96	739
Minimum	0.02	0.05	2.39	1.29
25 <sup>th</sup> percentile	0.6	2.8	15.5	12.7
75 <sup>th</sup> percentile	3.5	23.8	96.3	75.5

**Table 4.** Sensitivity, Specificity, Predictive value of negative, Predictive value of positive, Accuracy of patients in Group B, C and D ( the Threshold of Tg/ I-131 uptake ratio is 12.81ng/ml/%)

	Group B	Group C	Group D
Sensitivity	41.38%	88.37%	76.47%
Specificity	100%	100%	100%
Predictive value of negative	73.85%	86.49%	96%
Predictive value of positive	100%	100%	100%
Accuracy	77.92%	88.93%	96.46%

**Table 5.** The use of Tg/ I-131 uptake ratio threshold of 12.81 ng/ml/% to identify new patients from 1998 (not included in this study)

Group of patients	Tg/ I-131 uptake ratio ≥ 12.81 ng/ml/%(case,%)	Tg/ I-131 uptake ratio ≤ 12.81 ng/ml/% (case)
A	8 (100%)	0 ( 0% )
B	2 (33.33%)	4 ( 66.67% )
C	0 ( 0% )	3 ( 100% )

## DISCUSSION

Thyroglobulin is a large homodimeric glycoprotein molecule. Three factor determine serum Tg concentration in most clinical situations thyroid cell mass,<sup>2,3</sup> 1. physical damage to the thyroid caused by biopsy,<sup>4</sup> surgery,<sup>5</sup> hemorrhage,<sup>6</sup> radioiodine administration,<sup>7</sup> or 2. inflammation<sup>8</sup> and 3. activation of TSH-receptors by either TSH, chorionic gonadotropin (hCG)<sup>9</sup> or thyroid-stimulating antibodies (TSAb).<sup>10</sup> Tg is present in most differentiated thyroid carcinomas and some anaplastic thyroid carcinomas.<sup>11,12</sup> Among patients with thyroid carcinoma, serum Tg concentration are usually higher in those with follicular carcinoma than in those with papillary carcinoma, probably because follicular carcinoma are more advanced at the time of diagnosis.

The treatment of choice for differentiated thyroid cancer ( papillary or follicular carcinoma) is total or near total thyroidectomy. In most of this is followed by radioactive iodine treatment and thyroxine (T4) therapy. I-131 therapy has been

used for ablation of any remaining thyroid tissue and treatment of metastatic thyroid carcinoma. Serum Thyroglobulin (Tg) and I-131 whole body scintigraphy are suitable tumour markers for differentiated thyroid cancer after total thyroidectomy by surgery and I-131 ablation or treatment to identify residual tumor, metastases or late recurrence. Before the first I-131 treatment Tg is not a reliable marker since it can also be originated from remnant tissue ,thyroid surgery or residual tumor. The pre-treatment total body scan with I-131 for detection of metastasis has limited value because even 5-mCi dose was sufficient to reduce the uptake of a therapeutic dose by 54%<sup>13</sup> and low dose may not possible to detect distance metastasis while during the patient had residual thyroid tissue. The treatment dose of I-131 is depend on status of the patient. Early detection of lymph node metastasis, distance metastasis or late recurrence before I-131 treatment are importance for optimal treatment dose of I-131. The sensitivity is relatively low for lymph node metastasis (41.38%). Low

Tg/ I-131 uptake ratio can be influenced by low serum Tg level or high I-131 uptake. Patients with lymph node metastasis (Group B) had slightly high Tg level as compare with distance metastases and high I-131 uptake. However most of lymph node metastasis was detected by pathological tissue section. The sensitivity for distance metastases and late recurrence are 88.37%, 76.47%, respectively. The result of this study show that Tg/ I-131 24 hours uptake ratio might serve as a prognostic marker immediately after thyroidectomy but before radioiodine therapy to identify high risk patients such as distance metastases or late recurrence.

## CONCLUSION

Tg/ I-131 24 hours uptake ratio might be useful for evaluation of the patients status after thyroidectomy before ablative radioiodine therapy, so that the patients will receive optimal treatment doses of radioactive iodine.

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