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# Retrospective Evaluation of Well Differentiated Thyroid Cancer Treatment Outcomes: 50 year experience at the University of Puerto Rico

Frieda Silva[1,*], Reinaldo Laguna-Figueroa[1], Margarita Ramirez-Vick[2], Juan C. Negrón[1], Reynold López[3], José R Vázquez-Selles[1]

[1]Nuclear Medicine Section, Radiological Sciences Department School of Medicine, University of Puerto Rico

[2]Endocrinology section, Department of Medicine School of Medicine, University of Puerto Rico

[3]Surgical Oncology Section, Department of Surgery School of Medicine, University of Puerto Rico

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**Corresponding author:**

Frieda Silva, Nuclear Medicine Section, Radiological Sciences Department School of Medicine, University of Puerto Rico.

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## Abstract

Our study gathered information on the diagnosis, treatment, and long-term outcome in adult and pediatric Hispanic patients with Well Differentiated Thyroid Cancer.

*Methods*

We performed a retrospective review of the clinical and imaging nuclear medicine records of cases of WDTC evaluated and treated in the Nuclear Medicine CLINICc. Evaluation included the clinical PROFILE, histology, radioiodine (RAI) therapies and treatment response, long-term outcome and survival. The data was ASSESED using the 2015 ATA Risk level guidelines and recommendations.

*Results*

Three hundred eleven cases were reviewed, 81% females, 19% males, median age of 41 years. Eleven percent (34 patients) of the patients were in the pediatric group and 49% were between 16-45 years. The tumor histology was 60.5% Papillary, 28.2% Papillary-Follicular variant and 11.3% Follicular type. All patients had a total thyroidectomy. A total of 287 (92%) of the patients were treated with RAI. The median RAI dose was 128 mCi. Patients in the low risk group received a dose range of 25-105 mCi, 73 cases in the intermediate RISK group received 106-160mCi and 104 cases in the high-risk group received doses greater than 160 mCi. The overall median cumulative dose was 151 mCi (55-926 mCi). Annual follow up was done in all cases , WITH A median follow-up OF 5-10 years. Residual functioning tissue in the neck was found in 52% of the cases by US and/or RAI imaging. of those, 43% belonged to the low risk group, while 57% were in the intermediate and high-risk groupS. The mean treatment dose received by those with persistent functional thyroid tissue in the neck was 157 mCi.

Recurrent disease was found in 15% of the patients, 85% of them belonged to the intermediate and high -risk GROUPS. Forty-seven percent of the patients with recurrent disease had residual disease.

*Conclusion*

We believe ablative and/or adjuvant RAI treatment early in the disease is important to decrease residual thyroid tissue and/or residual disease, and to improve disease-free survival. We recommend total thyroid surgery in all tumors above 1 cm, post-operative evaluation with RAI Whole Body (with 123-I or 131-I), planar and SPECT/CT imaging and RAI ablation to remnant tissue. Follow-up post treatment evaluation is also recommended.

**Introduction**

For more than a century, thyroid malignancies have been one of the more extensively investigated tumors. Well differentiated thyroid cancer (WDTC) is the most common neoplasia of the endocrine system, the sixth most common in adult females. It is the endocrine tumor with the second GREATEST increase in incidence in patients less than 65 years (1). Differentiated thyroid tumors arise from the follicular cells and comprise most of the cases, the papillary type constitutes 85% of the group; follicular tumors and Hurthle cell ACCOUNT for the remaining 15%.

The increasing trend in the incidence of THISs tumor in the United States, Europe and Puerto Rico has been of interest in the past years. In Puerto Rico, the reported incidence of the tumor increased from 3.0 to 7.0/100,000 population from 1985 to 2004, the incidence rate being higher in females. The reported mean age at diagnosis in Puerto Rico is 47 years for women and 52 years for men (1).

In the past, treatment protocols included a total thyroidectomy to remove as much cancerous tissue as possible, and treatment with 131I to destroy or ablate any residual thyroid tissue, remaining tumor in the thyroid bed or surrounding tissue, and disease in lymph nodes or distant organs (2, 3). Nowadays, the American Thyroid Association (ATA) HAS set a more conservative management guideline for well differentiated thyroid tumors, endorsing conservative surgery and selective use of radioiodine (RAI) treatment. The European Thyroid Association (ETA) also dictated guidelines for differentiated thyroid cancer management, some of them in controversy with the American recommendations, especially those related to surgical extension and RAI ablation (4,5).

There is, however, extensive scientific literature demonstrating that long term prognosis of the disease, recurrence rate and disease control is related to the extension of the disease at diagnosis, the surgical approach, and the use of adjuvant radioiodine treatment.

For the past 50 years, our group has been evaluating, treating, and following a significant number of the well differentiated thyroid cancers in Puerto Rico using the existing recommendations for the time period. Our study gathered information during a fifty-year period on the diagnosis, treatments, and long-term outcome in a group of adult and pediatric Hispanic patients with Well Differentiated Thyroid Cancer. We STUDIED the population for their clinical characteristics, histology, RAI doses and treatment response, long-term outcome and survival. The data was EXAMINED retrospectively using the 2015 ATA Risk level guidelines and recommendations.

**Methods**

This is a retrospective review of the clinical and imaging nuclear medicine records of all cases of WDTC evaluated and treated at the Nuclear Medicine Section, Radiological Sciences Department of the University of Puerto Rico in San Juan, Puerto Rico.

Patients who had a total or near total thyroidectomy referred for evaluation to our Nuclear Medicine SECTION for RAI therapy were included in the study. Thyroid tumors were classified according to the American Joint Committee on Cancer (AJCC) guidelines. For this study, we used the 2015 ATA Risk of Recurrences Classification. Stimulated thyroglobulin (Tg) and thyroglobulin antibodies (TgAb) were assayed in most cases.

Patients were evaluated after surgery with a diagnostic 131-RAI Whole Body Scan before the RAI therapy. After the initial ATA guidelines were published in 2006, the 1131-RAI WBS was done POST -THERAPY.

Demographic data, tumor histology and staging were reviewed. The number and amount of ablative therapy, follow up studies and patient outcomes were tabulated and analyzed.

*Statistical Analysis*

The statistical software STATA version 11.0 (STATA Corp, College Station, TX) was used to perform the statistical analyses.

Descriptive statistics were used to describe the study population. Continuous variables were DEFINED using the mean, standard deviation, median and range. Frequencies and proportions were used to DEMONSTRATE categorical variables (sex, surgical procedure, extension of surgery, tissue remnants, histology type, TNM stage, metastasis (local, distant), disease status (disease free, residual or recurrent).

**Results**

A total of 311 cases were reviewed, 81% females and 19% males, with a median age of 41 years (4-96 years). Eleven percent (34 patients) of the patients were in the pediatric group and 49% were between 16-45 years. The tumor histology was 60.5% Papillary, 28.2% Papillary-Follicular variant and 11.3% Follicular type.

All patients had a total thyroidectomy. None of the patients had tumors less than 1 cm. According to the AJCC classification, 101 (34.3%) tumors were T2, 105 (34.3%) had nodal metastasis and 40 (13%) had distant metastasis .TABLE 1

When the ATA classification was used, 43% (n=130) of the patients were low risk; 27% (n=82) of the patients were intermediate risk and 30% (n=92) cases were high risk. However, when cases were separated into adult and pediatric (less than 15 years), 94% of the pediatric patients were in the high risk group and the remaining 6% were in the intermediate risk group (see Tables 2 ).

A total of 287 (92%) of the patients were treated with RAI. The median RAI dose was 128 mCi. Patients in the low risk group (110 patients), received a dose range of 25-105 mCi, 73 cases in the intermediate group received 106-160mCi and 104 cases in the high-risk group received doses greater than 160 mCi. The overall median cumulative dose was 151 mCi (55-926 mCi). TABLE 3.

Annual follow up was done in all cases, the median follow-up for 52% of the population was 5-10 years (range 5-43 years). A total of 143 patients were followed for 5 years, 80 cases were followed for 5-10 years and 76 patients for more than 10 years.

On the one-year evaluation, we determined “residual disease” (persistent radioiodine accumulation in the neck region) using a Whole-Body RAI Scintigraphy. After 2006, ultrasound evaluation of the neck was also performed.

Table 1. Staging -AJCC

| T Stage | % | N Stage | % | M Stage | % |
|---|---|---|---|---|---|
| T1 | 32.10% | N0 | 65.70% | M0 | 87% |
| T2 | 34.30% | N1 | 34.30% | M1 | 13% |
| T3 | 16% | | | | |
| T4 | 15% | | | | |

Table 2. Staging- ATA Guidelines

| | Low Risk | Intermediate Risk | High Risk |
|---|---|---|---|
| Adult | 130 patients | 82 patients | 92 patients |
| | 43% | 27% | 30% |
| Pediatric | 0 | 2 patients | 32 patients |
| | 0 | 6% | 94% |

Table 3. Treatment doses for each Risk Level blastocyst grades

| Risk Level | Cases | Treatment Doses |
|---|---|---|
| Low Risk | 43% | 50-105 mCi |
| Intermediate Risk | 27% | 106-160 mCi |
| High Risk | 30% | >160 mCi |

Table 4. Treatment Response grades

| | Low Risk | Intermediate Risk | High Risk |
|---|---|---|---|
| Residual Disease | 43% | 25% | 32% |
| Recurrent Disease | 12% | 41% | 47% |

Residual functioning tissue in the neck was found in 52% of the cases by US and/or RAI imaging. Of those, 43% belonged to the low risk group, while 57% were in the intermediate and high-risk group (Table 4). The mean treatment dose received by the group with persistent functional thyroid tissue in the neck was 157 mCi.

Recurrent disease was found in 15% of the patients, 86% of them belonged to the intermediate and high -risk groups. The sites for recurrent disease were the neck lymph nodes and the lungs. Forty-seven percent of the patients with recurrent disease had residual disease previously identified (see Table 4). The median therapeutic dose in this group of patients was 142 mCi of RAI.

At the end of the study, 98% of the population followed- up was alive. Fifty-two percent had persistent disease and 47.9% were free of disease. Disease-related mortality was 1.7% (5 cases), all of which had distant metastasis and belong to the high-risk group.

**Discussion**

Well Differentiated Thyroid Cancer, the most common endocrine tumor, is considered a slow growing, self-contained neoplasia. Even though the incidence of the tumor has been rising in the United States and Puerto Rico for the past 10 years, the mortality rate has remained low (1). In the past 10-20 years a

large number of publications address the management of these tumors Most of them emphasized radioiodine (RAI) treatment with the intent to eradicate disease and improve recurrence-free survival (3). The majority favors total thyroidectomy as primary treatment, followed by RAI ablation and thyroid hormone replacement.

In 2015 a group of experts from different specialties designed the American Thyroid Association (ATA) guidelines with a more conservative approach for the management of differentiated cancer (4), recommending total thyroidectomy as initial therapy only for tumors of 4cm or more. Recommendations were also published by the European Thyroid Association (ETA) and both were based on the risk of recurrences. However, the extent of surgical removal of the thyroid and the use of radioiodine for ablation are still today a matter of debate (5,6,7).

We reviewed our thyroid cancer patient data from the pre-ATA era to the post-ATA time. The characteristics of our population are similar to that reported in the literature, predominantly young females with papillary tumors. Eleven percent of our population was pediatric. As in previous reports, the group of pediatric cases presented with extensive disease at diagnosis, 94% of them presenting distant metastasis (ATA High Risk), and the remaining 6% belonging to the ATA Intermediate group. This number is higher than expected when we compare them to published data from other populations. This may be related to the fact that we are a tertiary care center (8,9,10,11).

When the 2015 ATA criteria were applied to the adult population, almost half of the cases (43%) were categorized as Low Risk, with T2N0 tumors. The remaining cases (57%) were graded in the high and intermediate group categories. Forty-eight percent of the patients had lymph node metastasis and/or distant metastasis at diagnosis.

In respect to initial treatment, all of our patients had total thyroidectomy. Thirty-two percent had a tumor stage T1b and 34% were stage T2, while none were less than 1 cm (Stage T1a). The multidisciplinary endo-surgical-nuclear group in our institution decided to continue the practice of total surgery (except for intra-thyroid micro carcinoma) and post-operative RAI ablation. This combination allows for adequate post-op treatment and follow up of the patients.

RAI therapy was administered to all cases, even those in the low risk group. The median treatment dose was 128 mCi, with a median maximum cumulative dose of 151 mCi. The lowest treatment dose administered was 50 mCi and was the dose given to those with residual functional tissue in the thyroid bed, 58% of the total population. Patients with distant metastasis to the lung (High Risk) received doses between 160-200 mCi. Among this group, there were 22 patients (21%) who received a total cumulative dose of 400 mCi. All of them were followed for more than 10 years. All are stable without evidence of secondary tumors or other radiation related complication. In general, treatment doses in 70% of the population ranged from 50 to 160 mCi.

According to the experience in our institution, we believe ablative and/or adjuvant RAI treatment early on in the disease is important to decrease residual thyroid tissue and/or residual disease, and to improve disease-free survival. Low dose ablative doses are recommended to low-risk patients without evidence of nodal disease at surgery and/or ultrasound, although since then we have adjusted the initial ablative dose in this group to 50-80 mCi.

A post-operative evaluation with RAI Whole Body scintigraphy and neck ultrasound is done in all cases. Suppressed serum Tg measurements are done at 6 and 12 months after initial ablative dose. This is considered important in the follow-up and further management and treatment dose decisions. The use

of RAI treatment provides the clinician an adequate opportunity to use the Tg and TgAb tumor markers in the follow-up of cases.

Recurrent disease in our cases was low (6%). We believe this is related to the multidisciplinary management, the initial extent of the surgery and the use of RAI. The survival of the patient group was, as expected, 98%, with only 1.7% of disease-related mortality.

**Conclusion**

In accordance with our experience and following recently published "Appropriate Use Criteria for Nuclear Medicine in the Evaluation and Treatment of Differentiated Thyroid Cancer", our group recommends total thyroid surgery in all tumors above 1 cm, post-operative evaluation with RAI Whole Body (with 123-I or 131-I), planar and SPECT/CT imaging and RAI ablation to remnant tissue. Follow-up post treatment evaluation with sonography, nuclear imaging and Tg and TgAb measurements is also recommended to decide follow-up and management (12).

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**References**

1. Ramirez Vick M, Nieves-Rodriguez M, Lugaro-Gomes A. Increasing incidence of Thyroid Cancer in Puerto Rico. PRHSJ, 2011; Vol 30, No 3
2. Middendop M, Grunwald F. Update on recent developments in the therapy of differentiated thyroid cancer. Semin Nucl Med, 2010; 40:145-152
3. Goldsmith S. To ablate or not to ablate: Issues and evidence involved in 131-I ablation of residual tissue in patients with differentiated thyroid carcinoma. Semin Nucl Med 41:96-104, 2011
4. Cooper D, Doherty G, Haugen B, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid: 26, No 1, 2016
5. Rondeau G, Tuttle M. Similarities and differences in follicular cell-derived thyroid cancer management guidelines used in Europe and the United States. Semin Nucl Med, 2011; 41:89-95
6. Verburg FA, Aktolun C, Chiti A, et al. Why the European Association of Nuclear Medicine has decline to endorse2015 ATA management guidelines for adult patients with thyroid nodes and differentiated cancer. Eur J Nucl Med. (2016) 43:1001-05
7. Grufride D., Giuffride R., Puliafito I, et al. Thyroidectomy as treatment of choice for differentiated thyroid cancer. International Journal of Surgical Oncology, Vol 2019, Article ID 2715260
8. Parisi M, Mankoff D. Differentiated Pediatric Thyroid Cancer: correlates with adult disease, controversies in treatment. Semin Nucl Med, 2007; 37:340-356
9. Handkiewicz D, Wloch J, Roskosz J et al. Total thyroidectomy and adjuvant radioiodine treatment independently decrease locoregional recurrence risk in childhood and adolescent differentiated thyroid cancer. J Nuclear Medicine 48: 879-888, 2007

10. Niedziela M. Pathogenesis, diagnosis and management of thyroid nodules in children. Endocrine-Related Cancer. 2006; 13: 427-453

11. Silva F, Laguna R, Nieves-Rivera F. Pediatric thyroid cancer with extensive disease in a Hispanic population: Outcome and long term survival. Journal of Pediatric Endocrinology and Metabolism 23: 59-64, 2010

12. Donohoe K, Aloff J, Avram A, et. al. Appropriate use criteria for nuclear medicine in the evaluation and treatment of Differentiated Thyroid Cancer. JNM Vol 61, No 3, March 2020