Effectiveness of different doses of radioiodine in differentiated thyroid cancer at the Hospital San Juan de Dios in Costa Rica

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Abstract

Objectives: to determine the effectiveness of different doses of radioiodine used as initial remnant ablation
Materials and methods: this is a prospective open label non randomized study. On August 2005 the Thyroid Clinic at the Hospital San Juan de Dios adopted a new treatment protocol. Patients were candidates for radioiodine therapy if they had age over 45 years, primary tumor maximal diameter over 1.5 cm, multifocality (3 or more foci), histological evidence of capsule, vascular or lymphatic invasion, lymph node metastasis or distant metastasis. Patients were graded according to the TNM classification. Patients with TNM I in which the only criteria was tumor size were offered 30 mCi of I131 (as outpatient). If the patient did not qualify for outpatient treatment, the patient was hospitalized and 50 mCi were given as treatment. For TNM II or above, 100 to 150 mCi were given on initial dose depending on histological characteristics.
Results: up to May 2008, 162 patients have been treated under this protocol. Epidemiologic characteristics are shown on table 1. 72 (44.4%) patients have had a follow up of at least one year with a whole body scan (WBS) and thyroglobulin levels using thyroid withdrawal protocol. Ablation effectiveness, defined as a negative WBS and a stimulated thyroglobulin level less than 2 ng/ml was achieved in 65% with 30 mCi of I131, 77,8% with 50 mCi, 47.1% with 100 mCi and 50% with 150 mCi. If we use only the negative whole body scan criteria (without stimulated thyroglobulin), overall success rate was 78.9% and there was no difference with different radioiodine dosis. Higher pre-ablation thyroglobulin levels predict a lower successful ablation rate.
Conclusions: With our current protocol, one year WBS was negative in 78.9% of patients, with no difference between TNM stages. However, when using WBS and thyroglobulin criteria, success was achieved in only 56.9%.

Introduction

Thyroid cancer is the most frequent endocrine cancer. Despite its frequency there is controversy about its best management strategy. Radioiodine treatment has been regarded as the main medical treatment available to prevent cancer recurrence.
The Thyroid Clinic at the Hospital San Juan de Dios in Costa Rica is a tertiary care center. We have been treating around 60 patients yearly with radioiodine for thyroid cancer. Starting on august 2005, we started collecting systematically the information of all these patients. In this abstract we present data on 72 patients that have been treated with any dose of radioiodine and have at least a 1 year follow up whole body scan.
We treat patients with radioiodine based on the following criteria:
- age over 45 years old
- tumor size greater than 1.5 cm
- more than 3 tumor foci
- vascular, lymphatic or capsule invasion (including microscopically)
- lymph node or distant metastasis
- extrathyroid invasion (either microscopically or macroscopically)
- high grade histological variants such as tall cell, insular

Radioiodine dose is selected based on the number of criteria the patient have, TNM staging, and socioeconomical situation. Patients over 45 years old and TNM I and those below 45 years old and no lymph node or distant metastasis are usually treated with 30 mCi unless social conditions render these patients not optmial for ambulatory treatment. In these cases, patients will receive 50 mCi as inpatient. Patients with lymph node metastasis and extrathyroid invasion are treated with 100 mCi and those patients with distant metastasis with 150 mCi.
All patients are treated using a T4 withdrawal protocol since we do not have rhTSH.
This is the first report on the success on remnant ablation of different doses of radioiodine following our current protocol.

Objectives

To determine the effectiveness of different doses of radioiodine used as initial remnant ablation

Materials and methods

This is a case series report. We assigned different doses of radioiodine therapy based on patient's clinical and histological characteristics. All patients are followed in our Thyroid Clinic. Effective remnant ablation is defined as a negative whole body scintigraphy and a stimulated thyroglobulin level below 2 ng/dl.

Information is analyzed using SPSS 15.0.

Results

72 patients are included in this study. Average age is 41.87 years (range 19-68). 88.9% are females. Tumor size on average is 1.93 cm ± 1.04 cm.

Graph 1. Initial surgical approach

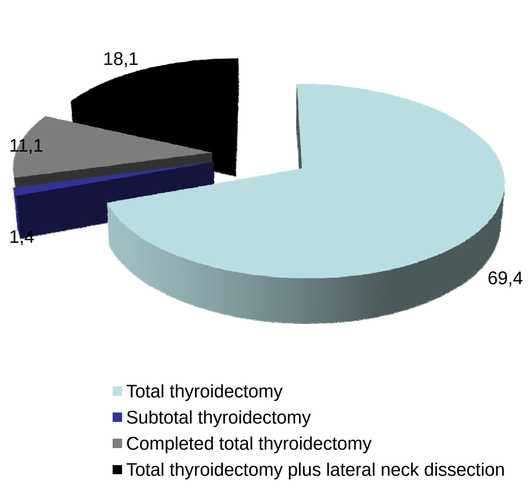


Table 1. Clinical and histological characteristics of differentiated thyroid carcinoma and TNM stage

	I % (n=107)	II % (n=24)	III % (n=27)	IVA % (n=4)	Total % (n=162)
Females	84.1 (90)	87.5 (21/24)	81.5 (22)	75 (3)	84 (136)
Age	37.07 ± 11.12	50 ± 11.31	54.48 ± 8.35	52.5 ± 4.93*	42.07 ± 12.84
Tumor size	2.02 ± 1.74	2.73 ± 0.76	2.11 ± 1.72	2.80 ± 2.15	2.16 ± 1.65
Lym-phatic invasion	20.6 (20)	14.3 (5)	17.1 (6)	50 (2)	21.6 (35)
Capsule invasion	52.3 (56)	41.7 (10)	59.3 (16)	100 (4)	53.1 (86)
Vascular invasion	29.9 (32)	29.2 (7)	22.2 (6)	75 (3)	29.6 (48)
Lymph node metas-tasis	30.8 (33)	8.3 (2)	37 (10)	75 (3)	29.6 (48)
Multifo-cality	26.2 (28)	29.2 (7)	25.9 (7)	25 (1)	26.5 (43)
Extrathy-roidal invasion	30.8 (33)	4.2 (1)	59.3 (16)	100 (4)*	33.3 (54)

* p<0.05

Table 2. Effectiveness of different doses of I131 by TNM stage, defined by a negative whole body scintigraphy and stimulated thryroglobulin less than 2 ng/dl

TNM Stage	30	50	100	150	Overall
I	68.8 (11/16)	75 (6/8)	43.5 (10/23)	50 (3/6)	58.6 (30/53)
II	33.3 (1/3)	100 (1/1)	25 (1/4)	--	37.5 (3/8)
III	100 (1/1)	--	66.7 (4/6)	100 (1/1)	75 (6/8)
IVA	--	--	100 (1/1)	0 (0/1)	50 (1/2)
Overall	65 (13/20)	77.8 (7/9)	47.1 (16/34)	50 (4/8)	56.9 (41/72)

Table 3. Effectiveness of initial radioiodine dose by TNM stage defined by solely a negative whole body scintigraphy

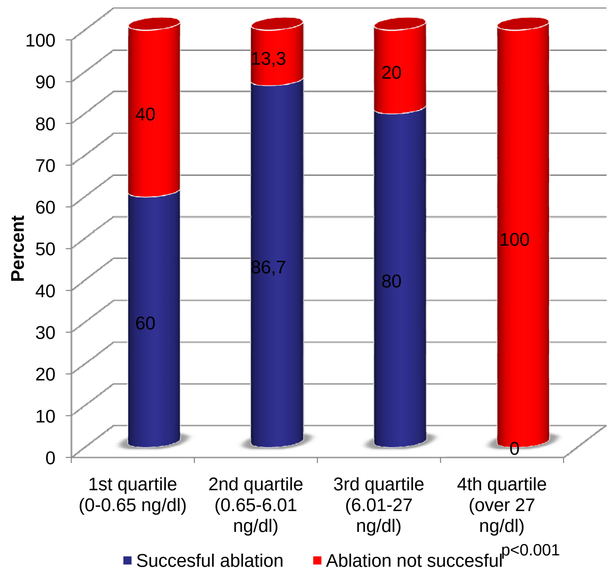
TNM Stage	30	50	100	150	Overall
I	75 (12/16)	75 (6/8)	82.6 (19/23)	83.3 (5/6)	58.6 (30/53)
II	33.3 (1/3)	100 (1/1)	50 (2/4)	--	50 (4/8)
III	100 (1/1)	--	100 (6/6)	100 (1/1)	100 (8/8)
IVA	--	--	100 (1/1)	100 (1/1)	100 (2/2)
Overall	70 (14/20)	77.8 (7/9)	82.4 (28/34)	87.5 (7/8)	78.9 (56/72)

Table 4. Comparison table between patients with and without successful remnant ablation

Characteristic	Successful remnant ablation (N=42)	Remnant ablation not successful (N=30)	P
Age (average ± SD)	44.49±11.04	38.30±10.50	0,020
Tumor size	1,65±0,92	2,30±1,10	0,009
Thyroglobulin level (on the day prior to I131 treatment, ng/dl)	5,13±6,27	102,43±180,18	0,003

There were no differences in gender, type of initial surgery, lymphatic invasion, vascular invasion, lymph node metastasis, multifocality, extrathyroid invasion, distant metastasis, presence of Hashimoto thyroiditis, TNM staging, I131 dose and days between surgery and radioiodine administration in predicting successful thyroid remnant ablation.

Graph 2. Thyroid remnant ablation success rate plotted by ablation thyroglobulin level



Discussion

This study shows an overall successful ablation rate of 56.9% at our center. This rate is a little bit better on lower doses of I131 (usually on TNM I or II) which is expected due to smaller amounts of remnant tissue. Bal et al reported no difference in ablation rates using 25-50 mCi of I131 but based on negative whole body scintigraphy or stimulated tyroglobulin less than 10 ng/ml. If we use the WBS negative criteria, then our remnant ablation rate would be the same as reported by Bal, at 77%. Stimulated thyroglobulin levels are more sensitive than WBS for the detection of recurrence. It is not unexpected that when we incorporate a more sensitive measurement that as thyroglobulin, our ablation success rate will be slightly lower.
International guidelines such as those issued by the European Association of Nuclear Medicine states that the effectiveness of ablation dose for 30-100 mCi are similar and right now there is no evidence that any dose is superior. Taking this in consideration, we are using the lowest ablation dose (30 mCi) specially for low risk patients. On higher risk patients, a higher dose is reasonable due to a higher chance of recurrence although this has not been clinically proven to make any difference. We are all aware that radioiodine therapy is not exempt on adverse events even on the long run such as second primary malignancies and higher cardiovascular risk (Brown et al 2008, Metso et al 2007) so we have to balance the long term risk benefit for these patients.
An expected finding is that pre-ablation thyroglobulin level will predict the successful ablation rate. We found that patients on the highest quartile (thyroglobulin higher than 27 ng/dl) will not achieve a follow up level of lower than 2 ng/dl. Higher thyroglobulin levels indicates a bigger amount of remnant tissue, which should render a lower ablation rate. Also, very high thyroglobulin levels may be caused by the presence of distant metastasis which may have not have been shown on an initial whole body scintigraphy. Therefore, ablation thyroglobulin level may be a variable to consider when deciding radioiodine dose.
We found that patients in which remnant ablation was not effective were younger and had a larger tumor size. Other factors such as lymph node metastasis were not statistically significant. This is in opposition of current risk stratification where age over 45 years is a risk factor for recurrence. A big difference is that we are just looking at successful remnant ablation and not clinical recurrence. Longer follow-up periods will be needed to see if these patients with remnant ablation not successful will have a higher recurrence rate. Radioiodine dose did not predict successful ablation rate, so we should be using the smallest possible dose.

Conclusions

A successful ablation rate of 56.9% is achieved using different doses of radioiodine (30-150 mCi). Lower TNM stages will achieve a higher ablation rate with lower doses of I131. Ablation thyroglobulin levels are a strong predictor of 1 year successful ablation rate.

References

1. Bal CS, Kumar A, Pant GS. Radioiodine dose for remnant ablation in differentiated thyroid carcinoma: a randomized controlled trial in 509 patients. J Clin Endocrinol Metab. 2004;89:1666-1673.
2. Brown AP, Chen J, Hitchcock YJ, Szabo A, Shrieve DC, Tward JD. The risk of secondary primary malignancies up to three decades after the treatment of differentiated thyroid cancer. J Clin Endocrinol Metab. 2008;93:504-515.
3. Metso S, Jaatinen P, Huhtala H, Auvinen A, Oksala H, Salmi J. Increased cardiovascular and cancer mortality after radioiodine treatment for hyperthyroidism. J Clin Endocrinol Metab. 2007;92:2190-2196.

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