

Original Article

Pediatric Differentiated Thyroid Carcinoma: Outcome in Response to Initial Treatment

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Abstract

Introduction: *Though the differentiated thyroid carcinoma in children is a common pediatric endocrine malignancy, its prognosis is excellent with a proper initial treatment.*

Objectives: *This is to evaluate the initial treatment pattern for a good prognosis with long-term outcome in pediatric DTC patients.*

Methods: *This study is a prospective one done in BSMMU during a period of 10 years in 52 post operative pediatric DTC patients after excluding the follow-up missing patients. These patients are yet in a regular follow-up were outcome evaluated with clinical, pathological & imaging studies.*

Results: *All the patients got initial treatment of total thyroidectomy. About half of the group had underwent neck dissection along with total thyroidectomy. Forty six patients had taken 131-I therapy. The survival is 100%.*

Conclusion: *The life expectancy for children with DTC is excellent. However, many patients experience adverse effects from thyroid surgery, resulting in life long complications.*

Keywords: *Differentiated thyroid carcinoma (DTC), Papillary thyroid carcinoma (PTC), Follicular thyroid carcinoma (FTC), Lymph node dissection (Neck Dissection).*

Introduction

Differentiated thyroid carcinoma (DTC), which comprises papillary thyroid carcinoma (PTC) and follicular thyroid carcinoma (FTC),

is a rare disease during childhood. However, DTC is the most common pediatric endocrine malignancy and its incidence is increasing¹⁻³. The prognosis in children has

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been reported to be excellent with 15 years survival rates greater than 95%³.

The biological behavior of the two carcinomas differ significantly where papillary thyroid carcinoma is known to frequently metastasizes to regional lymph nodes, where follicular thyroid carcinoma more frequently metastasizes to distant organs such as the lung, bone and brain. Pathogenesis of differentiated thyroid carcinoma is multifactorial with both genetic and environmental factors playing an important role⁴ For unknown reasons it was found to be 2-4 times more common in women⁵ Previous exposure to ionizing radiation including external irradiation of the neck would increase the incidence of cancer especially the papillary type.

Distant metastasis at the time of diagnosis is the most important prognostic factor for both papillary and follicular thyroid carcinomas⁶ Extra thyroidal extension and lymph node metastasis are important prognostic factors for papillary thyroid carcinoma while the grade of invasiveness and carcinoma differentiation are important to evaluate the biological behavior of follicular thyroid cancer⁷.

The initial treatment for children with DTC generally consists of a (near) total thyroidectomy with or without lymph node dissection, although for patients with minimally invasive PTC and lacking other adverse risk factors, a less aggressive treatment has recently been recommended^{8,9}

In most cases, surgery followed by ablation therapy with radioactive iodine (¹³¹I) to destroy residual tumor foci and to facilitate disease monitoring by follow-up scan and measurement of serum thyroglobulin¹⁰.

Aims & objectives

The objectives of this study were to evaluate the clinical and pathological characteristics,

response to initial treatment pattern, and long-term outcome of post operative DTC in prepubertal, pubertal, and post-pubertal patients i.e. pediatric patients.

Methods

This prospective study was conducted at Bangabandhu Sheikh Mujib Medical University, Dhaka, during, the period of January 2009 to December, 2018. Patients of DTC, age less than 18 years, admitted in the Department of Otolaryngology & Head-Neck surgery of this university and underwent surgery in this period of 10 years, were included in the study .

The data obtained from the medical file of each patient included the following: possible predisposing factors, e.g, hashimoto thyroiditis, familial DTC (first degree relative with DTC); previous exposure to external irradiation; presenting complaint and clinical findings; FNA cytology results; imaging, e.g, cervical US(ultrasonogram), computed tomography (CT) scan of neck and chest or magnetic resonance imaging (MRI) from diagnosis throughout follow-up from initial treatment (extent of operation. Operative findings, ¹³¹I dose) were recorded. Follow up given monthly for 6 months. Every three months for one year and then yearly.

Results

As shown in the study flow chart (Fig.1) 69 patients with pediatric DTC were identified and treated in our center, the ages ranging from 07 years to 18 years. Overall survival is yet 100% after a median follow-up of 4.5 years (range 0.3-10 years). Of the 69 survivors, 52 (75.4%) given informed consent and are included in this study. Among this study group 08 are male and 44 are female. Male; Female ratio is 15.38: 84.62. Median age at diagnosis is 14.3 years. At initial diagnosis, histologically confirmed

cervical lymph node metastases were found in 19 patients (36.54%) No distant metastasis found at diagnosis or in follow-up.

Total thyroidectomy was performed in all patients. In 32 patients (61.5%) the total thyroidectomy was performed as a single procedure. In the remaining 20 patients (38.5%), a diagnostic hemithyroidectomy was performed, followed by a completion thyroidectomy.

Lymph node dissection (Neck Dissection) was performed as part of initial therapy in 27 patients (51.91%) of which 19 (36.54%) were found positive for metastasis. These patients were underwent lateral neck dissection including levels II-IV±V on one or both sides of the neck (Table-1)

Forty seven patients underwent 131-I ablation therapy after surgery. Five patient did not receive 131-I therapy due to consultant's choice.

As shown in Table-2, post operative transient and permanent hypothyroidism were observed in 15(28.85%) and 2(3.85%) respectively. Both transient and permanent hypothyroidism occurred more often in patients who underwent a lymph node dissection. Unilateral RLN (Recurrent Laryngeal Nerve) injury occurred in 6 patients(11.59%). Bilateral RLN injury occurred only in a 13-years old patient who had treated with a total Thyroidectomy, a central compartment dissection and a bilateral Lymph node dissection. RLN injury occurred more often in patients with tumors staged T3-T4 compared with stage T1-T2(P<.001) and in patients with lymph node involvement (P<.001). The frequency of surgical complications did not differ between initial surgery performed before or during the last decade.

Table-I
Baseline Characteristics

Variable		All Patients (n=52)	0-10 yrs	11-14 yrs	15-18 yrs	P Value
Sex,n(%)	Male	8(15.38)	2(40)	4(22.2)	5(17.24)	.005
	Female	44(84.62)	3(60)	14(77.8)	24(82.76)	
Age at diagnosis,yr Median(range)	14.5(5-18)	8.5(5-10)	13.0(11.1-14)	17.2(15-18)	n.a	
Histopathology, n(%)	Papillary	40(76.92)	4(80)	14(77.77)	25(86.2)	.351
	Follicular	12(23.08)	1(20)	4(22.23)	4(13.8)	
Primary tumor size, cm Median (range)	2.5(1-5)	1.8(1-4.5)	2.9(1-5)	2.5(1-5)	.173	
Localization,n(%)	Unilateral	31(59.61)	3(60)	11(61.11)	18(62.06)	.364
	Bilateral	16(30.76)	1(20)	4(22.22)	7(24.13)	
	Other ^b					
	Isthmus	4(7.69)	1(20)	2(11.11)	4(13.79)	
	Thyroglossal duct	1(1.92)	0	1(5.55)	0	
Surgery,n(%)	Total thyroidectomy	52(100)	5(100)	18(100)	29(100)	n.a
Lymph node dissection	None	25(48.07)	3(60)	8(44.44)	14(48.27)	.045
	Central LND	02(3.84)	1(20)	1(5.55)	0	
	LND incl.	25(48.07)	1(20)	9(50)	15(51.72)	
	Lateral levels					

Abbreviation: LND lymph node dissection: n.a., not applicable.

^a Differences tested between the three age groups.

^b Summarized as one variable for statistical testing.

Table II
Surgical Complications

Group	Hypoparathyroidism, n (%)				Recurrent Laryngeal Nerve Injury, n (%)				
	None	Transient	Permanent	Unknown	None	Left	Right	Bilateral	Unknown
All Patients(n=52)	31(59.6)	15(28.85)	2(3.85)	4(7.69)	36(69.2)	3(5.77)	3(5.77)	1(1.92)	9(17.3)
T1-T2(n=33)	21(63.63)	11(33.33)	1(3.03)	0	28(84.84)	1(3.03)	1(3.03)	0	3(9.09)
T3-T4(n=19)	10(52.63)	4(21.05)	1(5.26)	4(21.05)	8(42.1)	2(10.52)	2(10.52)	1(5.26)	6(31.57)
No LND (n=25)	17(68)	7(28)	1(4)	0	19(76)	1(4)	1(4)	0	4(16)
LND(n=21)	10(47.6)	7(33.3)	0	4(19.04)	15(71.4)	2(9.5)	1(4.76)	0	3(14.28)
LND Unknown (n=6)	4(66.66)	1(16.66)	1(16.66)	0	2(33.3)	0	1(16.66)	1(16.66)	2(33.33)

Abbreviation: LND- lymph node dissection (Neck Dissection).

Outcome

At the time of the last evaluation, the survival was 100%. At this time point, 41 patients (78.85%) were disease-free. Outcome is similar in all age groups ($P=0.103$, data not shown). In 11 patients there is persistent disease or recurrence. Four patients (7.7%) have persistent disease, are classified as such based on a detectable Tg level. Six patients (11.54%) developed recurrence within 3.9 to 8 years after initial treatment. Of the five patients who had not been treated with ^{131}I after total thyroidectomy, one (1.9%) developed a recurrence of disease in the neck. Outcome did not differ between patients with PTC and FTC or between the three age groups.

Discussion

The recently proposed ATA risk of recurrence stratification system aimed to define the likelihood of recurrent or persistent disease after initial surgery in pediatric DTC and to identify the patients who would benefit from RAI treatment. In the present study, we demonstrated that the application of risk-stratification systems according to post-operative findings as well as the response to initial therapy, may facilitate predicting the disease course and outcome. The ATA risk-stratification system categorizes pediatric patients into three risk groups according to regional LN and distant metastasis staging

by using the tumor node classification system¹¹. However, it does not encompass all of the tumor characteristics necessary for accurate assessment of the prognosis after the diagnosis of DTC. In young children the relatively small thyroid nodule volume and its changes with age make it an unreliable prognostic criterion¹². The cumulative therapeutic ^{131}I activity during initial treatment and follow-up in our series was relatively high. Given the good survival rate, it can be questioned whether children could just as well be treated with lower therapeutic activities, as suggested by recent guidelines^{7,8}. It is our opinion that the administration of ^{131}I should be considered very carefully in pediatric patients to prevent possible early and late adverse effects^{13,14}. This especially the case in children with low-risk DTC because no benefit of ^{131}I ablation therapy has been shown in adults with low-risk disease¹⁵. High ^{131}I activities should be reserved for children with metastatic disease, as advocated earlier by Verburg et al¹⁶.

Strength and limitations

The major strength of our study is that the entire series was followed up at a single center by the same expert multidisciplinary team from diagnosis to the last visit. Thus all aspects of initial management were quite uniform, including extent of surgery, RAI

treatment, the degree of TSH suppression, and the rigorous surveillance protocol. The main limitations of our study are the relatively small series and relatively short follow-up period making it imperative that we continue to exercise caution and avoid generalizations when dealing with each individual case.

Conclusion

The life expectancy for children with DTC is excellent. However, many patients experience adverse effects from thyroid surgery, resulting in life long complications.

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