Surgical Treatment of Pediatric and Adolescent Papillary Thyroid Cancer: a Retrospective Study of 54 Patients in a Single Center

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Research

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Abstract

Background: In 2015, American Thyroid Association (ATA) issued the first version of *Management Guidelines for Children with Thyroid Nodules and Differentiated Thyroid Cancer.* The purpose of this study is to evaluate whether the ATA pediatric guidelines recommended surgical approach for the patient can be applied to surgical treatment of pediatric PTC in China.

Method: From April 2012 to December 2020, clinical data of children (≤18 years) with PTC consecutively admitted and treated with initial surgery in our department were retrospectively reviewed.

Result: A total of 54 children with PTC were enrolled in the study. We find that central lymph node metastasis (CLNM) rate was significantly higher than that in the lateral neck (83.33 % vs 62.96%，$\chi 2$= 5.704, p= 0.017), and the CLNM rate and LLNM rate both gradually increased with increasing of T stage. The lymph node metastasis rate was significantly lower in cN1b (-) patients than in cN1b (+) patient following routine CND (55.00% vs 100.00%, χ^2=15.263, p=0.000). Meanwhile, the CLNM and LLNM rates of ipsilateral were significantly higher than those of contralateral central compartment (83.33%vs 57.41%, χ^2=8.704, p= 0.003) and contralateral lateral compartment (62.96% vs 31.48%, χ^2 =10.737, p= 0.001). lymph nodes of 51 lateral LND from 34 children with cN1b (+) were analysed, which revealed the LNM rate of cN1b (-) patients was significantly lower than that of cN1b (+) patients (55.00% vs 100.00%, χ^2 =15.263, p=0.000). Meanwhile, the CLNM and LLNM rates of ipsilateral were significantly higher than those of contralateral central compartment (83.33%vs 57.41%, χ^2=8.704, p= 0.003) and contralateral lateral compartment (62.96% vs 31.48%, χ^2 =10.737, p= 0.001).

Conclusion: Pediatric and adolescent PTC is characterized with high involvement of CLNM and LLNM at the time of diagnosis. TT should be conducted in the majority of children with PTC, and lobectomy with isthmustomy should be selectively applied. CND should be routinely performed, therapeutic LND is recommended for children with cN1b (+), SLND including level II-V is preferred, and SSLND should be performed with caution. Based on single-center data, we believe that the 2015 ATA guidelines for children are applicable to the surgical treatment of PTC in domestic children.

Background

Although with a standardized incidence of 0.54 cases per 100,000 persons [1], differentiated thyroid cancer (DTC) is a rare disease in children and adolescents and contributes to about 1.4% of all pediatric malignancies. Furthermore, its incidence is rising [2–5]. The majority of thyroid cancer in children is DTC, including papillary thyroid carcinoma (PTC) and follicular thyroid carcinoma (FTC). Children are not small adults, as compared with adults, children PTC is characterized by larger tumor in size, higher prevalence of extrathyroidal extension (ETE) and lymph node metastasis (LNM) at the time of diagnosis [6, 7]. As PTC is rare in children, treatment approaches for pediatric PTC are historically extrapolated from adult experience, including American Thyroid Association (ATA) adult guidelines [8], the American Association of Clinical Endocrinologists [9], the National Comprehensive Cancer Network (NCCN) Guidelines(Version 2.2013), and the British Thyroid Association/Royal Physician Society Guidelines [10], etc. In 2015, ATA issued the first

version of *Management Guidelines for Children with Thyroid Nodules and Differentiated Thyroid Cancer* [11], which was confined to patients ≤ 18 years of age.

Surgery is still regarded as the most important treatment in children PTC. Due to the rarity of thyroid carcinoma in children and ethical concerns surrounding the clinical trials in such a population of underage patients, it is difficult to carry out prospective randomized clinical trial. Bhavani et al [12] recently reported that DTC in children managed according to adult guidelines had a good cure rate. As a result, this project retrospectively analyzed the clinical data of 54 children (aged ≤ 18) with PTC consecutively enrolled within the last 8 years, and followed-up, only then did we believe that the majority of pediatric PTC should perform TT, routine prophylactic CND and Therapeutic LND.

Patients And Methods

We retrospectively reviewed the medical records of 64 pediatric patients aged ≤ 18 years at the time of their initial visits and who were diagnosed with papillary thyroid carcinoma from April 2012 to December 2020 at the Department of Thyroid Surgery, the first affiliated Hospital of Kunming Medical University. 9 patients underwent initial surgery at another hospital were excluded, 1 patient was excluded due to incomplete pathological data.

Management Protocol

All patients underwent preoperative physical examination and high-resolution ultrasonography (US) evaluations of the thyroid gland and neck lymph nodes. Enhanced contrast CT scan was performed in patients with large primary tumor or extensive lymph node metastasis. US-guided FNAB of thyroid nodular or clinical involved nodes was not routinely performed preoperatively, while intraoperative frozen section pathological examination was routinely applied.

Total thyroidectomy (TT) was performed for children with bilateral tumors, multifocal tumors, primary tumors with T3 or T4 lesions, and clinical evidence of lymph node involvement or distant metastasis. Hemi-thyroidectomy (thyroid lobectomy with isthmusectomy) was selectively conducted in children with intrathyroidal solitary tumor < 1cm and no evidence of lymph node metastasis.

Central neck dissection (CND) was routinely performed in children with PTC confirmed by intraoperative frozen section, including therapeutic and prophylactic CND. Bilateral CND was performed in patients underwent TT, but ipsilateral CND was performed in patients with lobectomy. CND was implemented according to the CND consensus issued by ATA in 2009, including prelaryngeal nodes, pretracheal nodes and at least one paratracheal lymph nodes [13]. The medial boundary of unilateral CND is the medial edge of contralateral strap muscle, and unilateral CND includes prelaryngeal lymph nodes, pre-tracheal lymph nodes and ipsilateral paratracheal nodes.

Therapeutic lateral neck dissection was performed in patients with clinically apparent lateral nodal disease, which was defined as cN1b (+). cN1b (+) was diagnosed by preoperative physical examination, US, FNAB and intraoperative inspection, whereas no clinically apparent lateral nodal disease was defined as cN1b (-).

The scope of LND includes selective lateral neck dissection (SLND) in levels II-V or super selective lateral neck dissection (SSLND) in levels II-IV or levels III-IV. The LND specimens were separated according to neck levels before sent to department of pathology [14].

Individualized THS suppression therapy was performed in all patients with L-T4. Radioactive iodine therapy is recommended for children with T4, N1b or M1 disease. All patients were followed up regularly. Recurrences were defined as structural recurrence, and biochemical recurrences were excluded.

Data collection

As this study was conducted retrospectively, information on the following items was obtained: (1) Demographic characteristics (sex, age); (2) Surgical approaches, including the extent of thyroidectomy and lymph node dissection; (3) Data regarding the tumor characteristics(histology, primary tumor size, number and location, extrathyroidal extension and location of metastatic lymph nodes; (4) Surgical complications, including postoperative hemorrhaging, chyle leakage, permanent recurrent laryngeal nerve injury and permanent hypoparathyroidism; (5) Utilization of RAI and treatment outcomes.

The protocol of this study was reviewed and approved by the Institutional Review Board, and the study was performed in accordance with the Declaration of Helsinki.

Statistical analysis

SPSS17.0 statistical software was employed for data analysis. Continuous data were reported as mean ± standard deviation. Categorical variables were analyzed using Pearson's chi-square test. Two sided p values < 0.05 were considered statistically significant.

Results

Clinical Characteristics of the patients

The patient characteristics of 54 patients enrolled in this study are shown in Table 1. The subjects were 47 females and 7 males, with an average age of 14.93 ± 3.01 years and ranging in age from 6 to 18 years. The average disease course was 15.55 months (ranging from 4 days to 10 years).

The majority of children (50 cases) had classic PTC, 3 patients had diffuse sclerosing variant PTC, and 1 case of insular variant PTC. The average tumor size was 2.12 ± 1.14cm, ranging from 4 mm to 60 mm. 37 cases (68.52%) had solitary lesion and 17 patients (31.48%) had two lesions or more. 40 cases had unilateral cancer (74.07%) and 14 cases had bilateral carcinomas (25.93%). ETE was observed during thyroidectomy in 23 patients (42.59%).

According to the 8th version of AJCC tumor node metastasis (TNM) classification system, with proportions of T1, T2, T3 and T4 at 40.74% (T1a and T1b were 14.81% and 25.93%,respectively), 16.67%, 25.93% (1.85% of T3a and 24.07% of T3b, respectively), and 16.67% (all were T4a), respectively. At presentation, 45 patients (83.33%) had N1a disease, and 34 patients (62.96%) had N1b disease. Lung metastasis was found in 4 children (7.41%).

Table 1
Patients' characteristics

Characteristics	No. Of patients	%
Pathological type		
Classical PTC	50	92.59%
Diffuse sclerosing variant	3	5.55%
Insular variant	1	1.85%
Multifocality		
Single	37	68.52%
Multiple(≥2)	17	31.48%
Tumor location		
Unilateral	40	74.07%
Left lobe	23	42.59%
Right lobe	17	31.48%
Bilateral	14	25.93%
Tumor size		
≤ 1cm	13	21.07%
>1, ≤2cm	17	31.48%
> 2, ≤4cm	21	38.89
> 4cm	3	5.56%
extrathyroidal extension		
Yes	23	42.59%
No	31	57.41%

[a] For N classification, N0 no any evidence of regional lymph node metastasis; N1a and N1b were proved pathologically.

[b] For M classification, M0 no any evidence of distant metastasis; M1 was confirmed by Rx-WBS

Characteristics	No. Of patients	%
T classification		
T1	22	40.74%
T1a	8	14.81%
T1b	14	25.93%
T2	9	16.67%
T3	14	25.93%
T3a	1	1.85%
T3b	13	24.07%
T4a	9	16.67%
T4a	9	16.67%
T4b	0	0
N classification [a]		
N0	9	16.67%
N1a	45	83.33%
N1b	34	62.96%
M classification [b]		
M0	50	92.59%
M1	4	7.41%

[a] For N classification, N0 no any evidence of regional lymph node metastasis; N1a and N1b were proved pathologically.

[b] For M classification, M0 no any evidence of distant metastasis; M1 was confirmed by Rx-WBS

Lymph node metastasis based on T stage

We analyzed the relationship between T stage and lymph node metastasis (Table 2), and observed that lateral lymph node metastasis (CLNM) rate and lateral lymph node metastasis (LLNM)rate increased with

the increase of T stage of tumor. Only 12 cases were diagnosed as cN1a (+) and 34 cases as cN1b (+), preoperative and postoperative pathology revealed significantly higher CLNM rate than LLNM rate (83.33% vs 62.96%, $\chi 2 = 5.704$, $p = 0.017$). No skip metastasis was observed. LNM rate peaked to 100% in patients with T3 or T4 disease.

Table 2
Relationship between LNM rate and T stage

T-stage	N	CLNM [n/%]	LLNM [n/%]	LNM [n/%]
T1	22	14/63.64%	8/36.36%	14/63.64%
T1a	8	3/37.50%	2/25.00%	3/37.50%
T1b	14	11/78.57%	6/42.86%	11/78.57%
T2	9	8/88.89%	5/55.56%	8/88.89%
T3	14	14/100.00%	12/85.71%	14/100.00%
T3a	1	1/100.00%	1/100.00%	1/100.00%
T3b	13	13/100.00%	11/84.61%	13/100.00%
T4	9	9/100.00%	9/100.00%	9/100.00%
T4a	9	9/100.00%	9/100.00%	9/100.00%
T4b	0	—	—	—
Total	54	45/83.33%	34/62.96%[#]	45/83.33%

[#] compared with CLNM rate, $\chi 2 = 5.704$, $p = 0.017$.

Lymph node metastasis based on clinical N stage, surgical approaches

According to surgical records, 10 patients underwent hemi-thyroidectomy and 44 patients accepted TT;10 patients performed unilateral CND (2 patients with TT) and bilateral CND in 34 patients (2 patients underwent TT); LND were performed in 34 patients (unilateral LND in 17patients and bilateral LND in 17patients).

In this retrospective study, CND was routinely performed in cN1b (-) patients, while therapeutic LND was performed in cN1b (+) patients. We analyzed the relationship between clinical N stage, surgical approaches and LNM (Table 3), which revealed the LNM rate of cN1b(-) patients was significantly lower than that of cN1b (+) patients (55.00% vs 100.00%, $\chi^2 = 15.263$, $p = 0.000$). CLNM and LLNM rates of cN1b (+) patients were both peaked to 100.00%. Meanwhile, the CLNM and LLNM rates of ipsilateral were significantly higher than those of contralateral central compartment (83.33%vs 57.41%, $\chi^2 = 8.704$, $p = 0.003$) and contralateral lateral compartment (62.96% vs 31.48%, $\chi^2 = 10.737$, $p = 0.001$).

Table 3
Relationship between clinical N stage, surgical approaches and LNM

Clinical N Stage	Surgical approaches	N	CLNM [n/%]		LLNM [n/%]		
			Ipsilateral [a]	Contralateral	Ipsilateral [a]	Contralateral	LNM (+) [%]
cN1b (-)	CND	20	11/55.00%	4/20.00%	—	—	11 55.00%
	Unilateral CND [b]	10	5/50.00%	—	—	—	
	Bilateral CND [c]	10	6/60.00	4/40.00%	—	—	
cN1b (+) [d]	LND [e]	34	34/100.00%	27/79.41%	34/100.00%	17/50.00%	34 100.00%▯
	Unilateral LND	17	17/100.00%	12/70.59%	17/100.00%	—	
	Bilateral LND	17	17/100.00%	15/88.24%	17/100.00%	17/100.00%	
Total		54	45/83.33%#	31/57.41%	34/62.96%※	17/31.48%	

[a] In patients with bilateral lesions, the larger side of the tumor is regarded as ipsilateral and the smaller side of the lesion as contralateral.

[b] 2 patients underwent TT with unilateral CND.

[C] 2 patients underwent lobectomy with bilateral CND.

[d] including 2 patients for subsequent operation developed from cN1b (-).

LND includes SSLND and SLND.

▯ compared with LNM in cN1b(-)patients, $p = 0.000$.

compared with contralateral CLNM, $p = 0.003$.

※ compared with contralateral LLNM, $p = 0.001$.

Lymph node metastasis rate in different lateral levels

We analyzed the LNM rate of 51 LNDs from cN1b(+) 34 patients by different levels (Table 4), and observed the lowest LNM rate in Level V (15.69%), which was significantly lower than that in Level II, III and IV ($\chi2 = 33.443$, $p = 0.000$; $\chi2 = 60.016$▯$p = 0.000$; $\chi2 = 45.351$, $p = 0.000$). The LNM rate in Level III was significantly higher than that in Level II (92.16% vs 2.55%, $\chi2 = 6.746$, $p = 0.009$), but no significant difference between sub-Level IIa and Level IIb was observed. We also observed no significant difference in metastasis rate between Level III and Level IV ($p = 0.138$).

Table 4

Lymph node metastasis rate in different levels of lateral neck

LND	side	LLNM [n/%]							
		Level II			Level III	Level IV	Level V		
		II	IIa	IIb			V	Va	Vb
SSLND (III-IV)	6	—	—	—	5 83.33%	5 83.33%	—	—	—
SSLND (II-IV)	11	6 54.55%	6 54.55%	3 27.27%	9 81.82%	8 19.51%	—	—	—
SLND (II-V)	34	31 91.08%	26 76.47%	18 52.94%	33 97.06%	29 85.29%	8 23.53%	2 5.88%	7 20.59%
Total	51	37 72.55%▯※	32 59.26%	21 38.89%	47 92.16%▯	42 82.35%▯	8 15.69%	2 3.92%	7 13.73%
▯ compred with LLNM rate in level V, *P*=0.000;									
※ compred with LLNM rate in level III, *P*=0.009. (Pathological findings from the second surgery were included in the analysis)									

Surgical complications

Unilateral recurrent laryngeal nerve was resected in 2 patients due to tumor infiltration. 1 patient underwent tracheotomy due to temporary paralysis of bilateral recurrent laryngeal nerve. Chylous leakage developed in 2 patients and was cured with non-surgical treatment. No permanent hypoparathyroidism and postoperative bleeding occurred.

Follow-up and outcome

All children were treated with TSH suppression therapy with L-T4. 24 children underwent radioiodine therapy. No patients died of the disease in this cohort of children with a median follow-up of 38.56 months, and 5 patients (9.26%) developed recurrences and reoperation was performed. Recurrences were observed in central compartment in 3, in lateral compartment in 5 and in remnant thyroid in 1, including overlapping cases. The 5 patients with recurrences consisted of 2 cN1b (-) patients and 3 cN1b (+) patients. There was no significant difference in reoperation rate between cN1b (-) and cN1b (+) children (9.09 vs 9.38%, $p = 676$). There was also no significant difference in recurrence rate between SLND and SSLND groups (0% vs 8.82%, $p = 0.287$).

Discussion

Thyroidectomy

Surgery is the most important method to treat PTC, which ranges from lobectomy to total thyroidectomy (TT) [15]. There were no surgical treatment guidelines specific for children with thyroid carcinoma in China, and only adult guidelines can be referred to. The 2015 ATA pediatric guidelines recommended TT for the majority of children with PTC. The rationale for this recommendation is based on multiple studies showed an increased incidence of bilateral and multifocal lesions (30% and 65%, respectively) [16, 17], while a near-TT or TT can greatly reduce the risk of recurrence and subsequent second surgery [18–20]. TT can also optimize or reduce the utilization of postoperative ^{131}I treatment, and benefits serum Tg as tumor marker to detect recurrent or persistent lesions. In our study, the bilateral and multifocal lesions were 23.81% and 30.95%, respectively, which was lower than that quoted in ATA children guidelines [17, 21].

According to ATA adult guidelines [8], NCCN guidelines(Version 2.2020)and ATA pediatric guidelines [11], DTC patients with LNM should be treated with TT. Our results revealed that LNM rate in central and lateral compartment were 83.33%and 62.96%, respectively. Palaniappan et al reported LNM rate 71.6% [22]. Thus, based on high LNM rate, TT should be conducted in the majority of children with PTC.

Although TT is recommended for the majority of children with PTC, the extent of thyroidectomy is still controversial. The main problem is the influence of surgical resection scope on tumor recurrence and potential complications (such as transient/permanent postoperative hypoparathyroidism and recurrent laryngeal nerve injury) [19, 20, 23, 24]. Wang et al [25] reported that TT can not reduce recurrence, but only increase the surgical complications. Kluijfhout et al [26] proposed lobectomy as an option for ATA low-risk patients. Spinelli et al [23] believed that lobectomy could be applied in patients with unifocal lesion without distant metastases. Sugino et al [27] considered lobectomy with prophylactic unilateral CND was acceptable for patients without the risk factors of recurrence. Another study by Sugino et al [28] believed lobectomy may be sufficient as the initial surgical procedure for low-risk pediatric patients [no risk factors related to poorer DFS, cN1, ETE, and NMLNs (≥ 10)]. In fact, it is difficult to make accurate risk stratification and the recurrence risk of each patient pre-operatively or intra- operatively. There is no quantitative index to find the best balance between the risks and benefits of surgery.

In this study, we performed TT for children with bilateral lesions, multifocal tumors, locally advanced (T3 or T4) tumors and clinical evidence of lymph node or distant metastasis, and 10 patients with lobectomy and isthmus resection were selected (including T1a in 5, T1b in 4 and T2 in 1). The CLNM rate was revealed to be 50% pathologically in those 10 patients, and subsequent operation (remnant thyroidectomy) should be considered according to guidelines. We did not perform reoperation, TSH suppression therapy was conducted and 1 patient recurred during follow-up. There are no serious or permanent complications occurred in patients performed TT in this study. Therefore, we believe that the majority of children PTC should be treated with TT, and lobectomy be considered for a few patients with caution.

Central Neck Dissection

Central lymph nodes metastasis are common in PTC patients. Literatures reported that PTC in children were more likely to have CLNM [25, 29, 30], which increased the risk of pulmonary metastasis [17, 31, 32]. CND is

associated with a decreased risk of locoregional persistent or recurrent disease, so as to increase disease free survival (DFS) [33], as well as the potential to increase the efficacy of ^{131}I treatment [17, 34]. Additionally, some studies have shown that TT with prophylactic CND can increase 5-year and 10-year DFS to 95% [35]. It is recommended in ATA children guidelines [11] that CND should be performed in children with malignant cytology and clinical evidence of gross extrathyroidal invasion and/or locoregional metastasis on preoperative staging or intraoperative findings, and prophylactic ipsilateral or bilateral CND should be selectively considered in patients with no clinical evidence of gross extrathyroidal invasion and/or locoregional metastasis.

Owing to the possibility of permanent hypoparathyroidism following CND, some authors argued that CND in children with DTC is controversial. Unfortunately, there are no intraoperative data that reliably to predict which patient is at increased risk of locoregional metastasis or recurrence. Rubinstein et al [36] reported that LNM ratio > 0.45 may predict the likelihood of recurrence in pediatric PTC patients undergoing TT with prophylactic CND.

CND was routinely performed in our study, and the results revealed the CLNM rate in ipsilateral and contralateral of central compartment were 83.33%and 57.41%, respectively, and the CLNM rate in patients with T1, T2, T3 and T4 tumor were 63.64%, 88.89%, 100and 100, respectively.

Our data also revealed the CLNM rate in cN1b (-) and cN1b (+) patients were 55.00% and 100%, respectively. Study by Machens et al [37] showed that TT plus prophylactic CND can significantly decrease the need for subsequent surgeries, which was as high as 77% for patients without CND. Rubinstein et al [38] found a trend toward lower recurrence in patients undergoing thyroidectomy with CND compared with thyroidectomy alone in cN1b (-) patients ($p = 0.07$). Kim, et al [39] reported that tumor ≥ 1.1cm, ETE and multifocality are the independent risk factors for LNM, and suggested careful evaluation of the central compartment intraoperatively, so as to perform CND. However, as preoperative ultrasounds and intraoperative palpation are difficult to make an accurate assessment on the lymph node. In our study, only 12 (22.22%) patients were cN1a (+), and CLNM was confirmed to be 88.33% following routine CND. Recurrences were revealed in contralateral central compartment in 2 patients underwent lobectomy with unilateral CND and 1 in patient underwent TT, bilateral CND and bilateral LND patient. No permanent hypoparathyroidism occurred in this cohort of children.

Based on the high prevalence of lymph node involvement and difficulties in evaluating central compartment, we suggest prophylactic bilateral CND for PTC children underwent TT. Otherwise, prophylactic unilateral CND is acceptable for children underwent lobectomy.

Lateral Neck Dissection

Consensus has been reached on therapeutic LND for DTC patients [14]. Literature showed that therapeutic LND is associated with a reduction in persistent or recurrent disease and improved DFS in children [11]. The 2015 ATA children guidelines also recommended therapeutic LND, including Levels III, IV, anterior V, and II, and routine prophylactic LND is not recommended [11]. Ito et al [40, 41] suggested prophylactic LND for children with risk factors of lateral nodes involvement.

In current study, therapeutic LND (including SSLND or SLND) was performed on the basis of the preoperative evaluation by physical examination, US and CT, and results show that the LLNM rate gradually increased with the increase of T stage, and the LLNM rate in patients with T1, T2, T3 and T4 tumor were 36.36% (T1a: 25.00%, T1b: 42.86%), 55.56%,85.71%100%, respectively. Our results indicate the importance of preoperative evaluation. For this cohort of patients, our data also revealed 62.96% and 31.48% of LLNM in ipsilateral and contralateral of lateral neck, respectively; 100% of LLNM was observed in 34 cN1b (+) patients. Jeon et al [42] recently revealed that LLNM was independent predictors for structural persistent or recurrent disease.

We observed lowest LNM rate in Level V (15.69%), which was lower than in Levels II, III and IV ($p = 0.000$). The LNM rate in Level III was significantly higher than in Level II, but no significant difference between sub-Level IIa and IIb. We also observed no significant difference in metastasis rate between Level III and Level IV. As it is a retrospective study, some patients underwent SSLND (Levels II-IV dissection in 6 procedures and Levels III-IV dissection in 11 procedures), which was inconsistent with the recommendations of ATA children guideline. This may be due to the arbitrary decision by the surgeon, and someone will argue that the un-dissected nodes with occult metastasis would result in recurrence in patients underwent SSLND. Excellent outcome was reached with 38.56 months of follow-up, no significant difference in reoperation rate was observed between cN1b (-) and cN1b (+) children (9.09 vs 9.38%, $p = 676$), and no difference in recurrence rate between SLND and SSLND groups (0% vs 8.82%, $p = 0.287$) was observed. Such excellent outcome in this study may be due to non-randomized LND procedure or short follow-up time, and this group of patients are also being followed up.

Based on ATA guidelines recommendation [11] and our data, we also suggest therapeutic LND for pediatric PTC with clinical lateral lymph node involved, and SLND is preferred other than SSLND.

Conclusions

Our retrospective study data showed that pediatric and adolescent PTC is characterized with high involvement of CLNM and LLNM at the time of diagnosis. The CLNM and LLNM rates increased with the increase of T stage of primary tumor, and the CLNM and LLNM rates in the ipsilateral side of primary tumor were significantly higher than those in the contralateral side. Careful preoperative assessment of primary tumor and neck lymph nodes should be carried out to optimize the surgical approach. The majority of pediatric PTC should perform TT, and lobectomy be selectively applied. Prophylactic bilateral CND is prefered in patients who underwent TT, and unilateral CND is acceptable in patients with high risk of surgical complications and those with hemi-thyroidectomy. Therapeutic LND is suggested for children with cN1b (+) patient, SLND (Levels II-V) is preferred other than SSLND (Levels II-IV or Levels III-IV). Long-term follow-up is also particularly important.

Abbreviations

PTC: Papillary Thyroid Cancer; DTC: Differentiated thyroid cancer; FTC: Follicular thyroid carcinoma; ETE: Extrathyroidal extension; LNM: Lymph node metastasis; CLNM: Central lymph node metastasis; LLNM: Lateral lymph node metastasis; CND: Central neck dissection; LND: Lateral neck dissection; SLND: Selective lateral neck dissection; SSLND: Super selective lateral neck dissection; TSH: Thyroid stimulating hormone;

DFS: Disease free survival; NMLNs: Number of metastatic lymph nodes; TT: Total thyroidectomy; FNAB: Fine needle aspiration biopsy; TNM: Tumor node metastasis; AJCC: American Joint Committee on Cancer; US: Ultrasonography; NCCN: National Comprehensive Cancer Network; ATA: American Thyroid Association;

Declarations

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Authors’ contributions

YJS and SHC was involved in this study from the inception to design, acquisition of data, data cleaning, data analysis and interpretation, and drafting and revising of the manuscript. MZ, WL, CD and YHM was involved in project administration, principal supervision, and revising the final manuscript. JQ and RCC was involved in data cleaning and analysis as well as revising the whole work of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

All procedures performed in studies involving humanparticipants were in accordance with the ethical standards of theinstitutional and with the 1964 Helsinki declaration and its lateramendments or comparable ethical standards. Informed consent has been obtained from the patient's family for publication.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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