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Age-dependent reference values of the thyroid gland in pediatric population; from routine computed tomography data

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ABSTRACT

Purpose: To evaluate age-dependent reference values for measurements of the thyroid gland in pediatric patients.

Method: In total 425 chest and neck computed tomography images of pediatric patients without pathology of the thyroid gland were retrospectively reviewed. Measurements of the thyroid gland were obtained in three dimensions (width, depth, length). The total volume was the sum of volumes of each lobe. Measurements were compared among the six groups according to age from 0 to 18 years.

Results: There were moderate to strong positive linear correlations between age and all values (r = 0.58–0.82, all $p < 0.001$). The total volume of the thyroid gland showed a strong positive linear correlation with the three linear measurements of each lobe (all $r > 0.7$, all $p < 0.001$). Among these measurements, the depth of the right lobe showed the highest Pearson correlation coefficient with the total volume of the thyroid gland (r = 0.859).

Conclusion: The depth of right lobe could be a representative measurement of total thyroid gland volume, similar to prior findings in adults.

1. Introduction

Measurement of the size of thyroid gland is necessary for the diagnosis and treatment of thyroid diseases. Palpation of the thyroid gland is a necessary step in patients with suspected thyroid disease and is considered a screening test during physical examination. Ultrasonography (US) is known to be an accurate, safe, and noninvasive technique for thyroid gland evaluation (1). Although palpation is primarily used for goiter diagnosis, it is more accurate to measure the volume by using US. The World Health Organization (WHO) classifies the size of goiter using inspection and palpation into four grades. The method of palpation for thyroid size assessment has been criticized in many studies for its inaccuracy, and the US is known to be an accurate, safe, and noninvasive technique for thyroid gland evaluation and universally utilized method [1–4]. Several studies have measured the size of the thyroid gland by using US, and thyroid volume has been proposed as a criterion for assessment of thyroid size [5–9]. The WHO has provided reference values for thyroid volume by US for goiter screening in school-aged children (age range, 6–12 years) [9]. However, there are some limitations with respect to the use of US in children. First, it is difficult to measure the length of the thyroid, which is required for calculation of thyroid volume, because the short neck in children makes positioning of the linear probe used for thyroid US examination difficult. Second, in children who exhibit lack of cooperation, it is often difficult to accurately obtain all numerical values required to calculate thyroid volume. Together, these limitations cause difficulty in evaluating thyroid volume using US in pediatric patients. In adults, the depth of the thyroid gland measured using US is known to be the most accurate indicator of its volume. If the depth of the thyroid is > 2 cm, it is considered to be enlarged [4]. The volume of pediatric thyroid gland increases with age [10,11], making it difficult to apply the adult standard and there is a lack of reference values for pediatric population The thyroid gland is present in chest or neck computed tomography (CT). Some studies have measured the dimensions of the thyroid gland in

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adults using chest or neck CT [12–15]. Although CT is not regarded as the modality of choice for evaluation of the thyroid gland, linear measurement data of the thyroid gland (obtained from CT scans that have already been taken) would provide helpful data for assessment of pediatric populations.

To our knowledge, only one study in Japan [16] has provided reference US values regarding the thyroid gland for each age or body surface area of children (n = 38,063; range, 0–19 years. Our study will be the first to perform thyroid size measurements using existing chest or neck CT images from pediatric patients. The aim of our study was to obtain age-matched reference values for normal dimensions of the thyroid gland based on chest and neck CT. Furthermore, we aimed to determine which of these measurement values shows the highest correlation with thyroid volume.

2. Materials and methods

2.1. Patients

The institutional review board of our institution approved this retrospective study and waived the requirement for informed consent. We performed a retrospective review of chest and neck CT images for various disease other than thyroid gland diseases. The data was collected from a population between the ages of 0 and 24 years between March 2014 and February 2017 from the tertiary hospital in Daejeon, Korea. The initial dataset included data on patients up to 24 years of age. When the mean values of the measured dimensions and volumes were compared by dividing the patients into eight groups in increments of 3 years of age, none of the values showed statistically significant differences among the 15–18 year, 19–21 year, and 22–24 year groups. Therefore, we decided to obtain age-dependent reference values for the pediatric thyroid gland in patients up to 18 years of age. A total of 425 patients (boys:girls, 268:157; mean age, 9.5 ± 5.4 years; range 0–18 years) were enrolled in this study, and were subdivided by age into six groups in increments of 3 years.

2.2. Image acquisition and analysis

CT scans were performed using Somatom Definition Flash or Sensation-64 (Siemens Healthcare, Forchheim, Germany). The scan parameters were as follows: 80–120 kVp; 20–200 mAs; pitch, 0.6–1.5; and collimation, 32 × 1.2 mm, 64 × 0.6 mm, and 128 × 0.6 mm.

Linear measurements of the thyroid gland (width, X; depth, Y; length, Z) were obtained on axial and coronal images. Cross-sectional and coronal dimensions of the thyroid lobes were measured at the level of isthmus (Fig. 1). The volume of each lobe was calculated using the following equation [17]: Volume = (X ∗ Y ∗ Z) ∗ 0.479. The total volume of the thyroid gland was regarded as the sum of the left and right thyroid lobe volumes.

2.3. Statistical analysis

Statistical analyses were performed using SPSS 21.0 for Windows (IBM Corp., Armonk, NY, USA). A p-value of 0.05 was considered to be statistically significant. All linear measurements and volumes of the thyroid gland were presented as mean ± standard deviation. Pearson's correlation coefficient was used to evaluate the correlation between age and each linear measurement, as well as between age and volume. A one-way analysis of variance (ANOVA) with a Tukey multiple-comparison post-hoc test was used to compare the linear measurements and volumes of the thyroid gland among the six groups. The significance levels of the post hoc tests were set at $p < 0.003$ to correct for alpha error related to multiple comparisons.

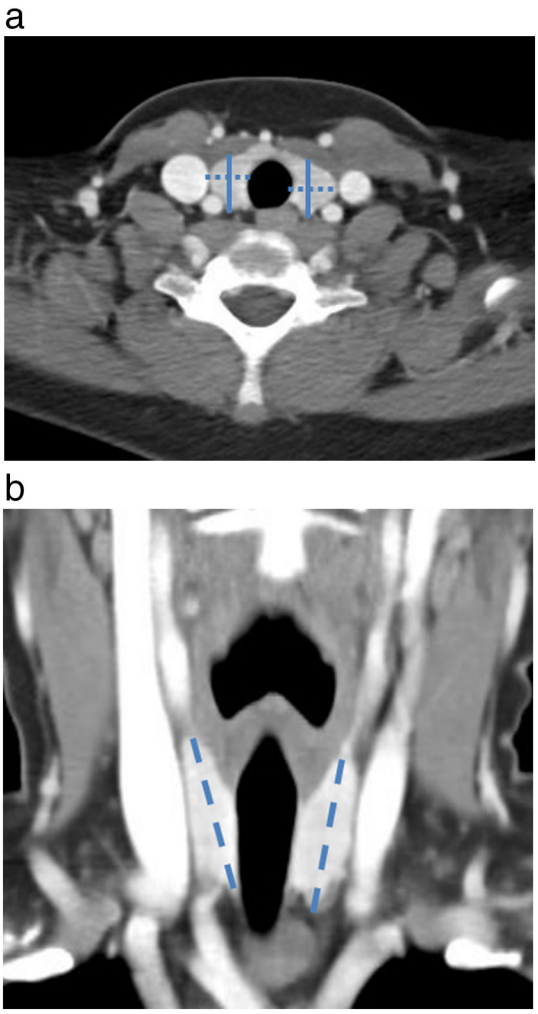

Fig. 1. Method of measurement performed on (a) axial and (b) coronal images of contrast enhanced CT. (a) Width: small dotted line, Depth: solid line, (b) Length: large dotted line.

3. Results

The descriptive statistics for the width, depth, length, and volume of each lobe, and the total thyroid volume in each group are presented in Table 1. Mean value of depth and volume of the right lobe were higher than those of the left lobe in all groups (all $p < 0.05$), except Groups 1 and 4. Moderate to strong positive linear correlations were observed between age and all values (r = 0.58–0.82, all $p < 0.001$). The mean values of linear measurements and volume of each lobe, as well as the total volume of the thyroid gland were statistically different among the 6 groups (Fig. 2). The total volume of the thyroid gland showed a strong positive linear correlation with the three linear measurements of each lobe (all $r > 0.7$, all $p < 0.001$). Among them, the depth of the right lobe showed the highest Pearson correlation coefficient with the total volume of the thyroid gland (r = 0.859, Fig. 3, Table 2).

4. Discussion

In this study, we obtained the thyroid volume and three linear measurements of width, depth, and length in Korean children (age range, 0–18 years). There were no differences in the ratios of boys and girls among the six groups. Moderate to strong positive linear correlations were observed between age and most measurements obtained in our study. All linear measurements and the volume of the thyroid gland increased as increased, up to 18 years of age. This result was similar to

Table 1
Mean values of linear measurements in three dimensions and volumes of the right and left lobes, total thyroid volume, and isthmic depth for different age groups among the pediatric population

Group (years)	Sex	Number	Age (mean ± SD, years)	Total volume (cm^3)	Right				Left				Isthmus
					Volume (cm^3)	Width (cm)	Depth (cm)	Length (cm)	Volume (cm^3)	Width (cm)	Depth (cm)	Length (cm)	Depth (cm)
0–3	M	47	1.4 ± 0.9	1.7 ± 1.0	0.8 ± 0.5	0.8 ± 0.2	0.9 ± 0.2	1.9 ± 0.5	0.8 ± 0.5	0.9 ± 0.2	0.9 ± 0.2	1.9 ± 0.5	0.1 ± 0.06
	F	27	1.2 ± 0.8	1.6 ± 0.6	0.8 ± 0.3	0.9 ± 0.2	0.9 ± 0.2	1.7 ± 0.4	0.8 ± 0.3	1.0 ± 0.2	0.9 ± 0.2	1.8 ± 0.4	0.2 ± 0.08
3–6	M	37	4.6 ± 0.7	3.6 ± 1.5	1.8 ± 0.9	1.1 ± 0.1*	1.2 ± 0.3	2.7 ± 0.5	1.7 ± 0.7	1.1 ± 0.1*	1.0 ± 0.2	2.7 ± 0.3	0.2 ± 0.06
	F	24	4.5 ± 0.8	3.2 ± 1.4	1.6 ± 0.8	0.9 ± 0.1	1.2 ± 0.3	2.7 ± 0.3	1.5 ± 0.8	1.0 ± 0.2	1.1 ± 0.3	2.7 ± 0.3	0.2 ± 0.08
6–9	M	41	7.4 ± 0.9	5.8 ± 2.3	3.1 ± 1.3	1.2 ± 0.2	1.6 ± 0.3	3.1 ± 0.4	2.6 ± 1.1	1.2 ± 0.2	1.4 ± 0.2	3.0 ± 0.4	0.2 ± 0.1
	F	19	7.3 ± 0.9	5.6 ± 1.9	3.0 ± 1.1	1.1 ± 0.1	1.6 ± 0.3	3.2 ± 0.5	2.5 ± 0.9	1.1 ± 0.3	1.5 ± 0.2	3.0 ± 0.5	0.2 ± 0.08
9–12	M	26	10.6 ± 0.8	6.9 ± 2.6	3.5 ± 1.4	1.2 ± 0.2	1.6 ± 0.3	3.3 ± 0.4	3.3 ± 1.3	1.3 ± 0.2	1.6 ± 0.3	3.2 ± 0.4	0.3 ± 0.1
	F	23	10.6 ± 0.8	7.8 ± 2.5	3.9 ± 1.4	1.2 ± 0.2	1.7 ± 0.2	3.5 ± 0.6	3.9 ± 1.3	1.3 ± 0.2	1.7 ± 0.4	3.4 ± 0.5	0.3 ± 0.1
12–15	M	53	13.4 ± 0.9	9.4 ± 3.4	5.0 ± 1.8	1.3 ± 0.2	1.9 ± 0.4	3.9 ± 0.7	4.4 ± 1.8	1.3 ± 0.2	1.7 ± 0.4	3.8 ± 0.6	0.2 ± 0.1
	F	41	13.7 ± 0.9	9.4 ± 3.3	4.9 ± 1.9	1.3 ± 0.2	1.8 ± 0.4	4.0 ± 0.7	4.4 ± 1.5	1.3 ± 0.1	1.7 ± 0.3	3.8 ± 0.5	0.3 ± 0.1
15–18	M	64	16.3 ± 0.8	12.5 ± 4.4	6.8 ± 2.7*	1.4 ± 0.2	2.0 ± 0.4	4.5 ± 0.6	5.7 ± 2.2	1.5 ± 0.3	1.8 ± 0.3	4.1 ± 0.7	0.3 ± 0.1
	F	23	15.8 ± 0.6	10.6 ± 3.6	5.5 ± 2.1	1.3 ± 0.2	1.9 ± 0.3	4.1 ± 0.7	5.1 ± 1.8	1.4 ± 0.2	1.7 ± 0.3	3.9 ± 0.4	0.3 ± 0.1

* Indicates a significant difference between boys and girls in the age group ($p < 0.05$).

those of previous studies that used US [8,10,16,18,19]. Marchie et al. [10] reported a sharp increase in the total volume of the thyroid gland between the ages of 13–15 years. Wiersinga et al. [11] reported that this increase in volume was associated with a sudden increase in thyroid size at puberty. Consistent with these findings [10,11], our study showed the most pronounced difference in linear measurements and volume of the thyroid between the age groups of 10–12 years and 13–15 years.

Most studies regarding thyroid volume in children have been performed on school-aged children (age range, 6–15 years) [5–9]. In our study, we analyzed data from pediatric patients between the ages of 0 and 18 years, and this is one an important strength of the study.

In this study the depth and the volume of right lobe were larger than those of the left lobe. In a similar study performed in Japan, the width, thickness, height, and volume of the right lobe were larger than those of the left lobe. They suggested that it may be affected by genetic factors or anatomical positioning of the thyroid gland, as the left lobe is usually located anterior to the esophagus [16].

Some studies have been performed previously regarding the linear measurements and volume of the thyroid gland in adults using chest or neck CT [12–15]. Nygaard et al. [12] reported a significant correlation between thyroid volume measured by US and CT ($r = 0.945$, $p < 0.005$). Hence, we believe that the measurements obtained in our study can be used as a reference standard for thyroid US in pediatric patients. In our study, the depth of the right lobe showed the strongest correlation with total thyroid volume. It is known that depth is important for determining enlargement of the thyroid gland on US in adults [4]. Our results show that the depth of the right thyroid lobe could be used to determine enlargement of the thyroid gland in pediatric patients. Although an international reference is provided for thyroid volume in children [5,9], various reference values have been described among countries [9,16,20,21]. Importantly, the present study provides reference values of the thyroid gland for Korean children.

When pediatric patients undergo thyroid US after clinical diagnosis of goiter by a clinician, we can evaluate thyroid gland size by applying reference values from our study. And the size of the thyroid gland evaluated based on our data and the size of the thyroid gland estimated by the clinician's inspection and palpation could be compared. Furthermore, we look forward to find the relationship between the reference values of thyroid gland and various laboratory findings (e.g., thyroid function test and antibodies).

There were some limitations to this study. First, this was a retrospective study, and we could not obtain data on height and weight, which can affect the volume of the thyroid gland. However, because the age of the patient can often be obtained more easily than the patient's height or weight while performing thyroid US in clinical practice, our results could be more useful for radiologists and clinicians who use US. Second, even though this study included patients without thyroid disease, we could not determine whether all patients were free of subclinical thyroid disease. We would like to compare normal children with pediatric thyroid disease patients, but it is difficult to perform CT in such patients. Third, this study used data from a tertiary hospital in one city (Daejeon) in Korea; thus, characteristics of the local environment may have biased the results. Further investigations and comparisons are needed, using data obtained from other parts of Korea.

5. Conclusion

Pediatric thyroid volume and linear measurements showed a tendency to increase until 18 years of age. The depth of the right lobe could be a representative measurement of the thyroid gland volume, in a manner similar to that used in adult examinations. The information obtained in this study is expected to be helpful for screening of the thyroid gland in the pediatric patients.

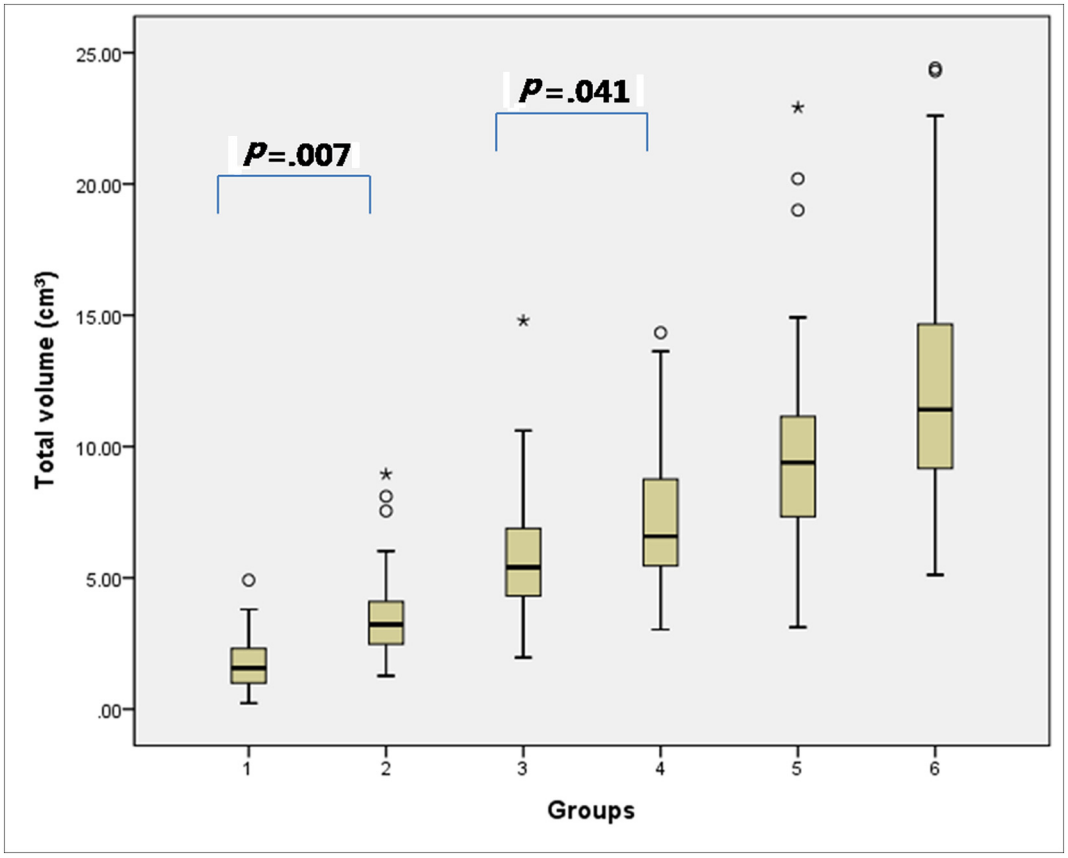

Fig. 2. Box plots of total volumes of the thyroid gland for the 6 groups.

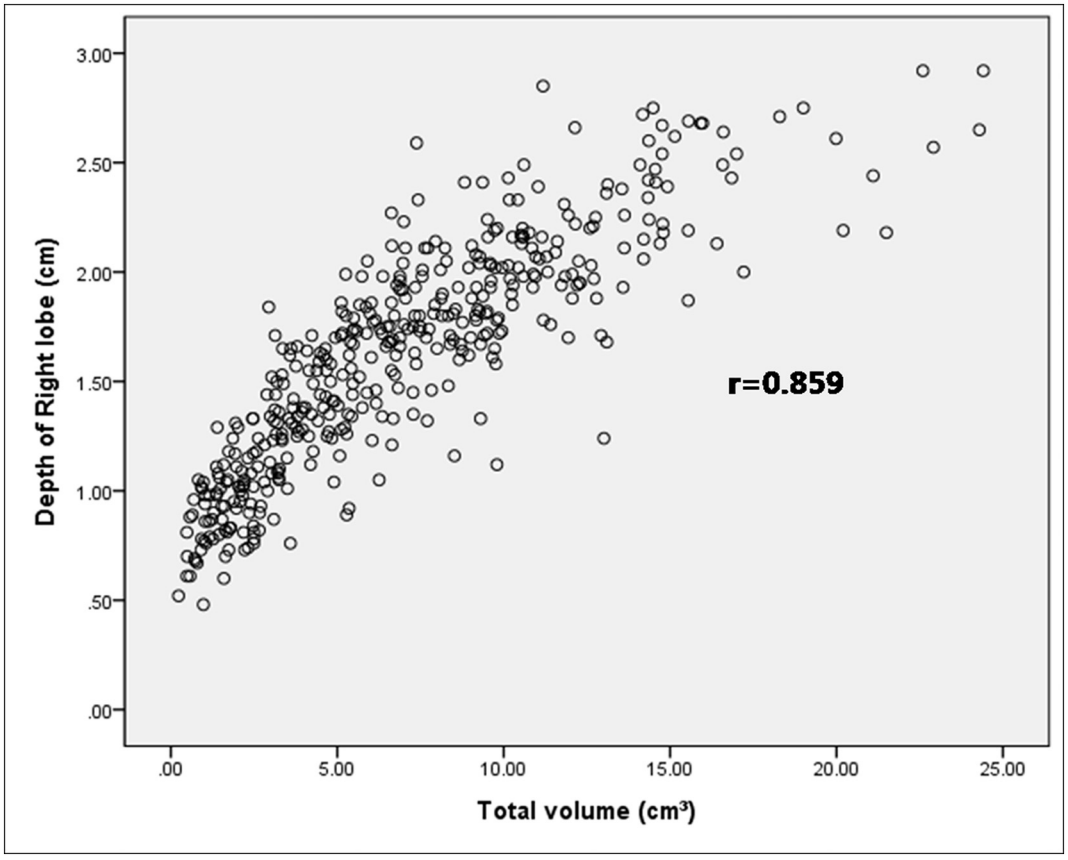

Fig. 3. Correlation between total volume of the thyroid gland and depth of the right lobe.

Table 2
Depth of right lobe of the thyroid gland in patients up to 18 years of age

Age (yrs)	Number	Mean (cm)	SD	Minimum (cm)	Maximum (cm)
0–1	26	0.87	0.17	0.52	1.12
1–2	24	0.97	0.20	0.48	1.31
2–3	24	1.07	0.28	0.60	1.66
3–4	15	1.01	0.23	0.76	1.63
4–5	22	1.22	0.37	0.70	2.02
5–6	25	1.41	0.26	0.90	2.01
6–7	25	1.54	0.21	1.08	1.94
7–8	12	1.74	0.35	1.29	2.41
8–9	22	1.70	0.36	0.92	2.49
9–10	13	1.76	0.20	1.34	2.05
10–11	17	1.70	0.30	1.04	2.11
11–12	20	1.76	0.36	0.92	2.34
12–13	26	1.72	0.36	0.89	2.41
13–14	29	1.97	0.45	1.05	2.72
14–15	38	2.01	0.40	1.16	2.85
15–16	47	2.11	0.39	1.21	2.92
16–17	23	1.87	0.35	1.32	2.64
17–18	17	2.16	0.43	1.24	2.75

Declarations of interest

None.

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