

Growth pattern and metastatic behavior of papillary thyroid cancer are similar in prepubertal children and adolescents

Machens A, Lorenz K, Thanh PN, Brauckhoff M, Dralle H. Papillary Thyroid cancer in children and adolescents does not differ in growth pattern and metastatic behavior. *J Pediatr* 2010. S0022-3476(10)00326-4 [pii];10.1016/j.jpeds.2010.04.026 [doi]

SUMMARY

BACKGROUND

Although uncommon, thyroid cancer is not unusual in adolescents and in the young adult population. Between 1975 and 2000, thyroid cancer represented approximately 7.8% of all cancers diagnosed in the 15- to 19-year age group according to data in the Surveillance Epidemiology and End Results (SEER) database (1). The yearly incidence of differentiated thyroid cancer (papillary and follicular thyroid cancer) in the United States in patients from 5 to 20 years of age ranged from 0.7 to 14 cases per year per million in patients 5 to 20 years of age (SEER 1975 to 2000) (1). The objective of the study by Machens et al. was to provide comprehensive clinicopathologic data, comparing the growth pattern and metastatic behavior of papillary thyroid cancer between children and adolescents.

PATIENTS AND METHODS

A total of 83 consecutive patients 18 years of age or younger had surgery for papillary thyroid cancer (PTC) from November 1994 through December 2009. A total of 36 patients had initial surgery and 47 had reoperations for suspected or confirmed locoregional disease, mainly lymph-node metastases. Of the 83 patients, 57 (69%) were women and 26 (31%) were men, comprising 9% of the 921 patients treated at the Martin Luther University, Halle (Saale), Germany, for papillary thyroid cancer during this period.

Five (6%) of the 83 patients, 9, 12, 14, and 15, and 16 years of age, had a history of external radiation for inoperable intrathoracic neuroblastoma, nephroblastoma (Wilms' tumor), Hodgkin's lymphoma, acute lymphocytic leukemia, and medulloblastoma 5 to 10 years earlier.

All 83 patients had total thyroidectomy, 80 of whom (96%) also had systematic lymph-node dissection, and 57 (69%) had lateral neck compartment dissection. In addition, the upper anterior mediastinum was dissected in 7 (8%) of the 83 patients. Three children did not have lymph-node dissection because they were incidentally found to have 4-, 6-, and 10-mm solitary PTCs, confined to the thyroid gland.

RESULTS

Clinicopathologic Patient Characteristics by Age Groups and Tumor Growth Pattern (Figures 1 to 4)

Among the 83 patients with PTC, there were no age-related difference in sex distribution, reoperation rate, history of external radiation, multifocal tumor growth, number of thyroid cancers, extrathyroidal tumor growth, lymph-node metastases, number of involved and removed lymph-node metastases, number of involved and dissected lymph-node metastases, or distant metastases (Figure 1).

After stratifying the tumor growth pattern, patients with extrathyroidal tumor growth were found to have larger tumors,

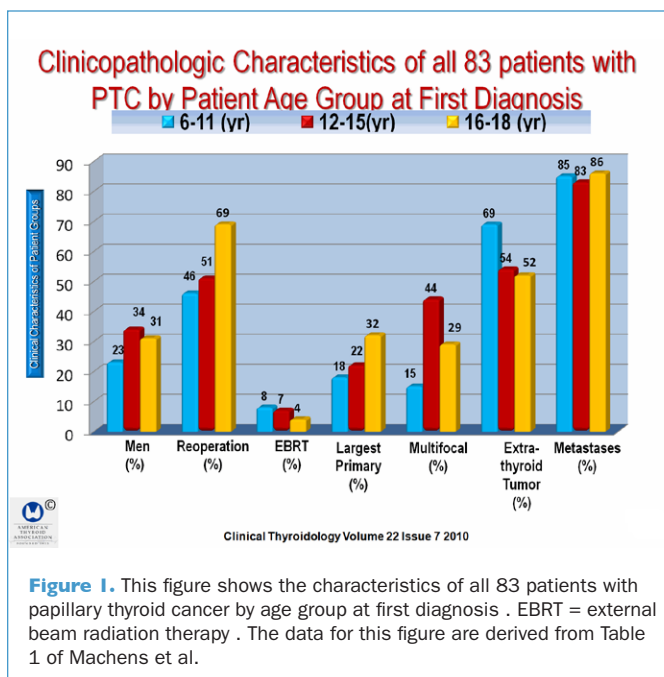


Figure 1. This figure shows the characteristics of all 83 patients with papillary thyroid cancer by age group at first diagnosis. EBRT = external beam radiation therapy. The data for this figure are derived from Table 1 of Machens et al.

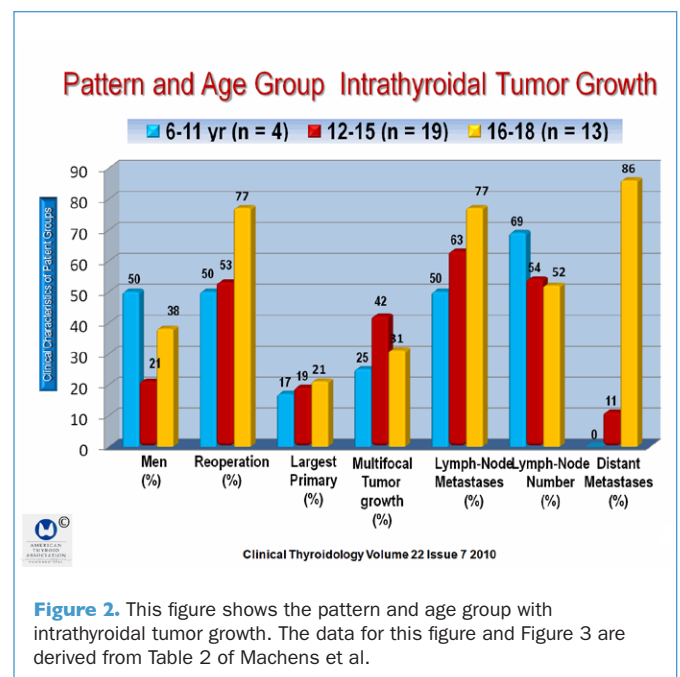


Figure 2. This figure shows the pattern and age group with intrathyroidal tumor growth. The data for this figure and Figure 3 are derived from Table 2 of Machens et al.

especially in the highest age group, but this difference was not significant (Figures 2 and 3).

When stratified by increments of 10 lymph nodes, significant relationships were found with the intensity of lymph-node metastases and multifocal tumor growth, the number of thyroid cancers, and extrathyroidal tumor growth. However, all

other clinicopathologic variables, including patient age at first diagnosis, did not differ significantly when grouped by the number of lymph-node metastases (Figure 4).

CONCLUSION

This study suggests that there is a similar growth pattern and metastatic behavior of PTC in prepubertal children and adolescents.

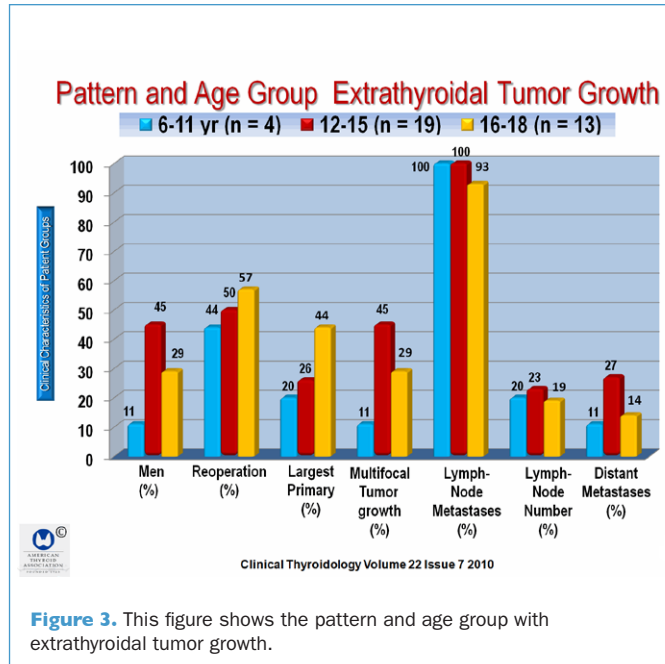


Figure 3. This figure shows the pattern and age group with extrathyroidal tumor growth.

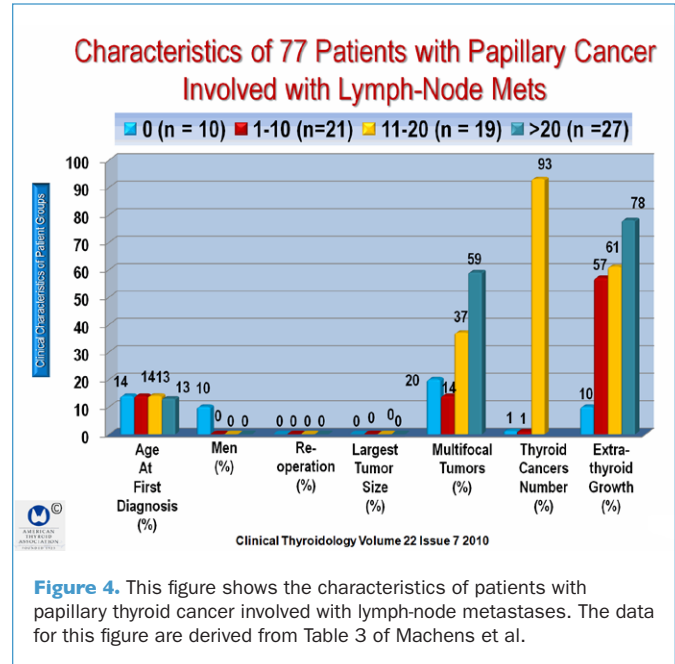


Figure 4. This figure shows the characteristics of patients with papillary thyroid cancer involved with lymph-node metastases. The data for this figure are derived from Table 3 of Machens et al.

COMMENTARY

Almost all the young patients in this study had lymph-node metastases and extrathyroidal tumor growth without a significant difference between prepubertal children and adolescents. The authors suggest that typically, children and adolescents with locoregional metastases trigger a workup for thyroid cancer and prompt referral for specialist surgical care, introducing referral and age bias in studies (2,3). The authors make the point that if children had more extensive disease as compared with adolescents, the children should have been overrepresented among the pediatric patients in this study, which apparently is not the case. However, this is a relatively small study that may not have been large enough to uncover minor age-related differences among the two study groups. The authors conclude that having comparable extent of disease, children should not receive less extensive neck surgery as compared with adolescents, which may result in a higher rate of locoregional recurrence in young children. A study of 19 patients by Robie et al. (3) found a strong trend toward locoregional recurrence among those with metastatic disease to more than five cervical nodes (P<0.08); however, the primary operations on the thyroid and regional nodes were not significant predictors of neck recurrence. Although there have been no deaths among these patients, 25% had persistent disease at a mean follow-up of 12.6 years, leading the authors to conclude that the incidence of surgical morbidity

does increase with more extensive surgery, and that outcome is predicted primarily by the initial extent of disease. Likewise, Machens et al. also suggest that the extent of the initial operation is what influences locoregional recurrence rates rather than the child's age; however, they provide the caveat that with surgery in children and adolescents, and especially in younger children, there is more of a risk than in older patients, and thus should be treated by dedicated surgical centers that have experience with pediatric neck surgery.

SEER Database Information on the Incidence Rates and Mortality Rates in Children and Adolescents, and Young Adults (Figures 5, 6, and 7)

A SEER monograph (1) of cancer epidemiology in older adolescents and young adults (15 to 29 years of age) provides important insight into the epidemiology of thyroid cancer in children. The SEER data show that in the United States, from 1975 through 2000, thyroid cancer accounted for about 10% of all malignancies diagnosed in individuals 15 to 29 years of age, and thyroid cancer was the fourth most common cancer in this age group. The incidence of thyroid cancer increased rapidly between 15 and 29 years of age, reaching a plateau by the 5th and 6th decades (Figure 5).

In 2000, the estimated incidence rates of thyroid cancer per million in persons younger than age 30 years were 0 for age

<5 years, 1.0 for ages 5 to 9, 4.3 for ages 10 to 14, 17.6 for ages 15 to 19, 43.3 for ages 20 to 24, and 63.0 for ages 25 to 29 (Figure 6). Moreover, the estimated numbers of persons diagnosed with thyroid cancer in 2000 were 0, 20, 89, 335, 820, and 1222, respectively.

Based on incidence data collected from 1975 through 2000 in the U.S., approximately 2,400 persons between 19 and 29 years of age had a diagnosis of thyroid cancer. More than half these patients were 25 to 29 years of age. Over this same period, more than 350 older adolescents in the 5 to 19 year age group had a diagnosis of thyroid cancer. (4)

The estimated incidence rates of thyroid cancer in year 1975 through 2000 per million in persons younger than age 44 years, was 0 for age <5 years, to 78% in patients age 40 to 44 years. (Figure 6).

The mortality rate of thyroid cancer increased above the age of 10 years, and continued to rise as a function of age.

It is difficult to dismiss the effect of age on the outcome of papillary and follicular thyroid cancer, including that of prepubertal, pubertal and adolescent patients.

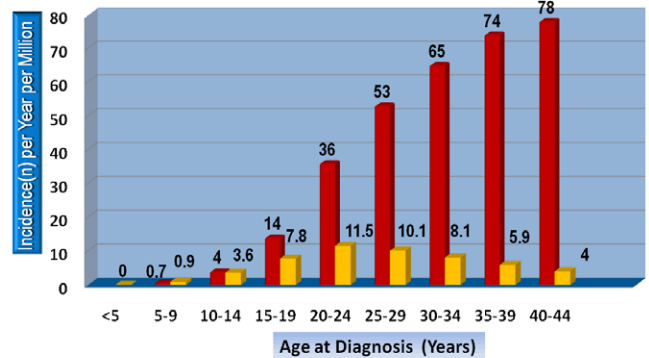
The mortality rate of thyroid cancer increased at greater than 10 years of age and continued to rise as a function of age (Figure 7). Mortality from thyroid cancer has not declined in the 15-

to 29-year age group during the past quarter century, probably because of the high survival rates (1).

It is difficult to dismiss the effect of age on the outcome of PTC.

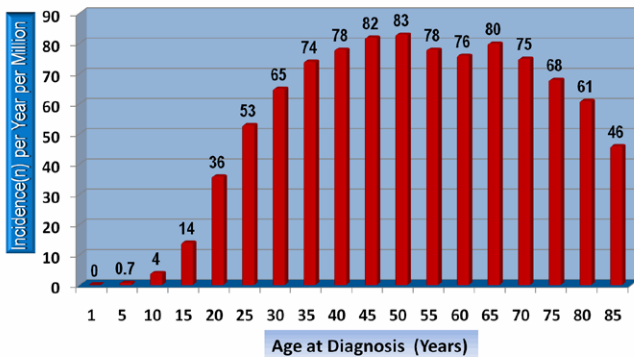
— Ernest L. Mazzaferri, MD, MACP

SEER Incidence of Thyroid Cancer Relative to all Cancer



Clinical Thyroidology Volume 22 Issue 7 2010
Figure 6. This figure shows the incidence rate per year per million of thyroid cancer relative to all other cancers by age (yr) at the time of diagnosis. The data for this figure are derived from SEER figure in chapter 12, figure 12.1, chapter 12, page 146. (4)

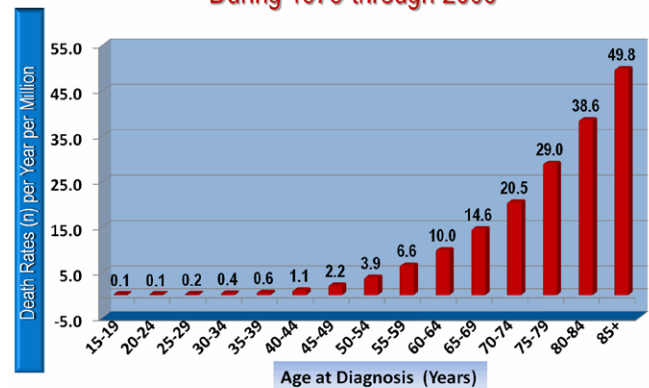
SEER Incidence of Papillary and Follicular Thyroid Cancer



Clinical Thyroidology Volume 22 Issue 7 2010

Figure 5. This figure shows the incidence rate per year per million, by age at the time of diagnosis of differentiated thyroid cancer (papillary and follicular thyroid cancer) from 1975 through 2000. The data for this figure are derived figure 12.3 in Chapter 12, page 147 in the SEER Monograph (1)

SEER Thyroid Cancer Deaths per Year per Million During 1975 through 2000



Clinical Thyroidology Volume 22 Issue 7 2010

Figure 7. Mortality from thyroid cancer has not declined in the 15 to 29-year age group during the past quarter century, probably because of the high survival rates (1). The data for this figure are derived from SEER figure 12.13 in chapter 12, chapter 12, page 150 (4).

References

1. Bleyer A, O’Leary M, Barr R, Ries LAG, eds. Cancer epidemiology in older adolescents and young adults 15 to 29 years of age, including SEER incidence and survival: 1975-2000. Bethesda, MD: National Cancer Institute, NIH publication no. 06-5767.
2. Machens A, Hauptmann S, Dralle H. Referral bias in thyroid cancer surgery: direction and magnitude. Eur J Surg Oncol 2008;34:556-62.

3. Machens A, Dralle H. Age disparities in referrals to specialist surgical care for papillary thyroid cancer. Eur J Surg Oncol 2009;35:1312-7.
4. Robie DK, Dinauer CW, Tuttle RM, et al. The impact of initial surgical management on outcome in young patients with differentiated thyroid cancer. J Pediatr Surg 1998;33:1134-40.