Journal of Pediatric Surgery 50 (2015) 1009–1013

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

Pediatric papillary thyroid cancer >1 cm: is total thyroidectomy necessary?

Tate Nice [a,*], Sebastian Pasara [b], Melanie Goldfarb [c], John Doski [d], Adam Goldin [e], Kenneth W. Gow [e], Jed G. Nuchtern [f], Sanjeev A. Vasudevan [f], Monica Langer [g], Elizabeth A. Beierle [a]

[a] Department of Surgery, Division of Pediatric Surgery, University of Alabama at Birmingham, Children's Hospital of Alabama, Birmingham, AL
[b] School of Public Health, University of Alabama at Birmingham, Birmingham, AL
[c] Department of Surgery, John Wayne Cancer Institute/Providence St. John's Medical Center, Santa Monica, CA
[d] Department of Surgery/Pediatric Surgery Division, University of Texas Health Science Center, San Rosa Children's Hospital, San Antonio, TX
[e] Division of General and Thoracic Surgery, Seattle Children's Hospital, Seattle, WA
[f] Division of Pediatric Surgery, Baylor College of Medicine, Houston, TX
[g] Division of Pediatric Surgery, Maine Medical Center, Portland, ME

ARTICLE INFO

Article history:
Received 26 February 2015
Accepted 10 March 2015

Key words:
Pediatric
Papillary thyroid cancer
Thyroidectomy

ABSTRACT

Purpose: Treatment of pediatric papillary thyroid cancer (p-PTC) often follows adult guidelines, including total thyroidectomy for tumors >1 cm. This study examined the association between operation type and overall survival (OS) for tumors >1 cm in size in the pediatric population.
Methods: Patients ≤21 years of age with primary papillary thyroid cancer >1 cm were reviewed from the National Cancer Data Base (NCDB) from 1998 to 2011. Kaplan-Meier analysis followed by Cox proportional hazard models estimated the impact of total thyroidectomy (TT) vs. partial thyroidectomy (PT) on overall survival. Models were adjusted for patient, tumor, and treatment factors.
Results: 3,861 cases (3474 TT, 387 PT) were included. Estimated 15-year overall survival was 96.10% after TT and 96.18% after PT ($p = 0.0855$). In multivariate analysis of 3173 patients, only lowest socioeconomic level (HR 4.93, $p = 0.001$) and unfavorable histology (HR 6.11, $p = 0.016$) were associated with worse OS. Survival for patients undergoing TT was not statistically improved over those undergoing PT (HR 0.81, $p = 0.694$).
Conclusion: p-PTC >1 cm has an excellent 15-year overall survival. Treatment with TT did not have an improved OS compared to PT. Lower socioeconomic status and unfavorable histology were associated with decreased OS.

Well-differentiated thyroid cancer remains the most common endocrine cancer in the pediatric population, ranging from about 1% of all pediatric malignancies in pre-pubertal children to 7% in adolescents [1]. It affects approximately 0.54 per 100,000 children each year, but the incidence seems to be increasing by 1.1% per year [2,3]. Most pediatric thyroid cancers are either papillary carcinoma or follicular variant of papillary carcinoma (FVPTC) [2].

Treatment of pediatric papillary thyroid cancer (p-PTC) often follows adult guidelines, including total thyroidectomy for tumors >1 cm. However, debate remains over which operation is optimal and whether adult standards should be applied to the pediatric population. This study utilized the National Cancer Data Base to examine the association of patient, tumor, and treatment characteristics to overall survival for p-PTC tumors >1 cm in size. A special focus was placed on type of operation in relation to overall survival.

2. Methods

2.1. Data source

The National Cancer Data Base (NCDB) is a data repository jointly maintained by the American Cancer Society and the American College of Surgeons Commission on Cancer. With over 1500 participating centers, approximately 70% of all cancer cases in the United States are captured in the database [4,5]. Data from the NCDB has been used in over 350 articles since 1990 [6]. Database records are created through accredited centers by using highly standardized methods and definitions, consistent with specifications by the North American Association of Central Cancer Registries. Records include patient characteristics, cancer properties, treatment administered, and basic outcome information. Data definitions are readily available online [7].

Abbreviations: FVPTC, follicular variant of papillary carcinoma; NCDB, National Cancer Data Base; OS, overall survival; p-PTC, pediatric papillary thyroid cancer; PT, partial thyroidectomy; TT, total thyroidectomy.

* Corresponding author at: University of Alabama at Birmingham, 1600 7th Avenue South, Lowder Building - Suite 300, Birmingham, AL, 35233. Tel.: +1 205 638 9688; fax: +1 205 975 4972.
E-mail address: Tate.Nice@childrensal.org (T. Nice).

http://dx.doi.org/10.1016/j.jpedsurg.2015.03.031
0022-3468/

2.2. Study cohort

Institutional review board exemption was obtained (E131009002). All patients ≤21 years of age with primary papillary thyroid cancer >1 cm were examined from the NCDB from 1998 to 2011. Entries with omission of survival data or those that did not undergo a surgical procedure were excluded.

2.3. Categorization

All histology codes consistent with papillary thyroid cancer and its subtypes were included: 8050, 8052, 8260, 8337, 8340, 8341, 8342, 8343, 8344, 8350, 8450, 8452, 8503, 8504, and 8507. Separate categories were created for FVPTC (8340) and unfavorable histology, which consisted of papillary squamous cell carcinoma (8052), insular carcinoma (8337), columnar cell (8344), diffuse sclerosing (8350), and solid pseudopapillary tumor (8452).

Patient race was classified as white, black, or other. The NCDB uses a second variable for Spanish or Hispanic origins, and this was categorized as either Hispanic or non-Hispanic. Socioeconomic status was estimated by using the average income for the patient's ZIP code based on 2000 US Census data and classifying into quartiles. Patient comorbidities were recording using Charlson/Deyo Comorbidity Index and were divided into 0, 1, and ≥2. The Charlson/Deyo Comorbitity Index is a standardized method of combining a patient's comorbidities, from 17 different categories, into a single score to help estimate risk from those conditions [8].

Tumor stage was determined by the NCDB analytic stage, which uses pathologic staging when known, otherwise clinical staging is used for the NCDB analytic stage. Clinical and pathological findings were both used to determine metastasis and nodal involvement. Extra-thyroidal extension was based on either a clinical or pathological T stage of 4, 4A, or 4B. Tumor size was based on pathology and categorized into 10–19 mm, 20–29 mm, and ≥30 mm.

Type of operation was classified as TT or PT, with PT including sublobar resection, lobectomy, or lobectomy with isthmectomy.

2.4. Statistical analysis

chi-Square and pooled variance t-tests were used to compare demographics, tumor characteristics, and treatments between groups. Kaplan-Meier survival estimates were calculated for TT versus PT patients and compared using the log-rank test. Cox proportional hazard models were used to compare survival between these groups adjusting for age, sex, number of comorbidities (Charlson/Deyo Score), race, income quartile, tumor size, unfavorable histology, follicular-variant histology, NCDB analytic stage, multi-focal disease, distant metastasis, extra-thyroidal extension, nodal status, and radioiodine treatment. Due to missing data, not all patients could be utilized for every variable analysis. Comorbidity index, nodal involvement, and multifocality had much lower rates of data completeness. While these variables did undergo univariate analysis, they were dropped from multivariate analysis. Statistical significance was determined at $p \leq 0.05$. Statistical analysis utilized SAS software, version 9.3 (Cary, North Carolina).

3. Results

A total of 3861 cases of p-PTC >1 cm with a known surgical procedure and known survival status were included in the analysis. Table 1 demonstrates the overall study population. The mean age was 17.6 years with most patients (83.9%) between 15–21 years of age. The majority were white (87.1%), non-Hispanic (79.6%), and female (82.5%). All income levels were represented, with 12.6% in the lowest quartile (<$20,000) and 43.6% in the top income quartile (>$46,000). Only 57 patients (1.5%) had unfavorable papillary histology, and 26.2% had follicular variant of papillary carcinoma. Tumors were most commonly greater than 3 cm in size (44.6%), while similar numbers of 1–2 cm (28.3%) and 2–3 cm (27.1%) were seen. Lymph node involvement occurred in 44.9% of patients, but extra-thyroid extension was seen in only 12.4%, and only 2.5% of patients had metastatic disease. Multifocal lesions were seen in 34.5%. 3474 (90%) patients underwent total thyroidectomy, while 387 (10%) were treated with partial resections. Of the partial resections, 354 (91.5%) were a lobectomy with or without isthmectomy and 33 (8.5%) were sublobar resections. Radiation, primarily radioactive iodine, was utilized in the treatment regime of 2353 (63.1%). Median follow-up was 83 months with a maximum of 179 months.

Table 1 also compares the total thyroidectomy and partial resection subpopulations. The populations had similar demographics, except the partial resection group had slightly higher percentages of non-white patients. Tumor size, stage, and amounts of unfavorable histology were similar between the two groups. Compared to the partial resection group, patients undergoing total thyroidectomy had less follicular variant of papillary cancer (23.5% vs 49.9%) and higher rates of lymph node involvement (47.6% vs 18.8%), extra-thyroid extension (13.2% vs 4.4%), metastasis (2.7% vs 0.5%), and multifocal disease (35.6% vs 22.7%). Patients in the total thyroidectomy group were also more likely to undergo radiation therapy (65.9% vs 37.9%).

A total of 48 deaths were recorded, 40 (1.15%) following TT and 8 (2.07%) after PT. Table 2 depicts univariate analysis for overall survival. Due to incomplete data entry, not all patients could be utilized for each variable analysis and the number analyzed for each variable can be seen in the table. NCDB analytic stage, comorbidities, unfavorable histology, and distant metastasis were each associated with lower OS ($p < 0.05$). Conversely, radioiodine therapy, female gender, and increasing socioeconomic status were associated with increased OS ($p < 0.05$). Other factors did not significantly impact OS. Specifically, operation type had no statistical association with overall survival in the univariate analysis ($p = 0.0911$). As seen in Table 2, lymph node status, multi-focal tumors and number of comorbidities were not entered for many of the patients. Therefore, these variables were dropped from the multivariate model due to the requirement for data completeness of all variables and the large drop in patient numbers that would have resulted to include these variables. The multivariate analysis included 3173 cases, and the results are shown in Table 3. Again, survival for patients undergoing total thyroidectomy was not statistically different than those undergoing partial thyroidectomy ($p = 0.6939$). Only lowest socioeconomic level (HR 4.93, $p = 0.001$) and unfavorable histology (HR 6.11, $p = 0.016$) were associated with worse OS.

Fig. 1 reveals the results from the Kaplan-Meier analysis of survival by operation type. Survival did not significantly differ between those undergoing TT versus those having PT ($p = 0.0855$). Estimated 15 year overall survival after TT was 96.10% and 96.18% after PT.

4. Discussion

This study encompasses the largest examination of pediatric papillary thyroid cancer to date. OS was excellent for pediatric patients with p-PTC >1 cm in size, with 15 year OS estimated to be above 96%. These data confirmed the good prognosis normally attributed to children and adults with papillary thyroid cancer. Upon initial review, the 40 deaths after total thyroidectomy may seem significantly higher than the 8 deaths after partial thyroidectomy. However, this difference is actually attributable to the much higher numbers of patients who underwent total thyroidectomy compared to those undergoing partial resection. In this study, univariate and multivariate analysis as well as Kaplan-Meier survival analysis all showed that pediatric patients who underwent TT for tumors >1 cm did not have an improved OS compared to those patients who received PT.

While the TT and PT groups were similar, there were differences in some of the tumor characteristics. Multifocal and lymph node disease were two of the variables that had the most missing information. Still,