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Original research

Surgical treatment for dominant malignant nodules of the isthmus of the thyroid gland: A case control study

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HIGHLIGHTS

- The aim of this study was to identify differences between PTC of the isthmus and the thyroid lobes.
- Another aim was to identify differences between PTC and microcarcinomas located in the isthmus.
- We retrospectively analyzed 2239 patients subjected to total thyroidectomy.
- PTC in the isthmus were more likely to be associated with multifocal disease lymph node involvement and capsule invasion.
- Total thyroidectomy could be considered as an appropriate surgical treatment for isthmic PTC.

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ABSTRACT

Backround: Appropriate surgical treatment of papillary thyroid carcinomas (PTC) located in the isthmus remains controversial. The aim of this study was to evaluate the clinicopathological characteristics of PTC of the isthmus compared to tumors located in the thyroid lobes, to identify differences between PTC and microcarcinomas of the isthmus, and to use these findings to establish total thyroidectomy as an appropriate surgical resection for treating these tumors.

Methods: We retrospectively analyzed 2239 patients subjected to total thyroidectomy. PTC was diagnosed in 575 patients, of whom 521 had dominant malignant nodule located in thyroid lobes and 54 had a dominant carcinoma located in the isthmus. Patients with isthmic PTC were divided in Group A ($n = 27$) with PTC >10 mm and Group B ($n = 27$) with microcarcinoma ≤10 mm.

Results: In univariate analysis, multifocality ($p = 0.019$), lymph node metastasis ($p < 0.001$), mean tumor size ($p = 0.028$) and age ≥45 ($p = 0.036$) were significantly associated with PTC with dominant nodule in the isthmus. Additional analysis of PTC groups (>10 mm vs ≤10 mm) in isthmus showed that multifocality, bilaterality, histological subtype and lymph node metastasis were not significantly different between the two groups.

Conclusions: Our results suggest that PTCs located in the isthmus were more likely to be associated with multifocal disease, lymph node involvement and capsule invasion, than carcinomas in other thyroid regions. Therefore, total thyroidectomy could be considered as an appropriate surgical treatment for papillary carcinomas located in the isthmus regardless of size.

1. Introduction

Papillary thyroid carcinoma (PTC) is the most common thyroid follicular cell-derived malignancy and is considered to be a relatively indolent tumor from which death is rare. However, in the elderly and in patients exposed to radiation, PTC can behave aggressively [1,2].

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Recent advances in ultrasonography screening and fine-needle aspiration biopsy (FNAB) have facilitated the detection and diagnosis of PTC. The increased accuracy of histopathologic examination, in particular with the number and thinness of the anatomical slices have resulted in a marked increase in the rate of preoperative diagnosis of papillary thyroid microcarcinoma (PTMC) [3–5].

The thyroid isthmus lies directly anterior to the trachea, overlying the second to fourth tracheal rings and is covered by the strap muscles, fascia, and skin in the middle of the neck. The frequency of isthmus nodules is uncertain. Only a few studies have reported a low prevalence (6.4%) of nodules located within the thyroid isthmus compared to nodules located in the thyroid lateral lobes [6]. Well differentiated carcinoma arising within such nodules of the isthmus among all malignant thyroid nodules reportedly range from 1% to 9% [7–10].

The surgical treatment for papillary thyroid carcinomas located in the isthmus remains controversial based on anatomical and biological characteristics. The American Thyroid Association (ATA), the British Thyroid Association (BTA) and the European thyroid Association (ETA) assigned recommendations for well-differentiated thyroid cancer, but there are no precise guidelines for the management of patients with dominant thyroid nodules of the isthmus [8,11,12].

Additionally, the management of papillary microcarcinomas in thyroid lobules has become a controversial topic the last years. PTMC treatment can range from a follow-up without surgery, to total thyroidectomy with or without iodine treatment [13–15]. To our knowledge, there are no specific guidelines for the surgical treatment of papillary microcarcinomas confined to thyroid isthmus.

In this study, we retrospectively analyzed the clinicopathologic characteristics of patients with dominant thyroid nodules of the isthmus in an attempt to identify differences between PTC and PTMC and also differences between PTC located in the isthmus and in other thyroid regions, aiming to examine whether total thyroidectomy is the surgical treatment that should be adopted for suspicious thyroid nodules of the isthmus regardless of their size.

2. Patients and methods

A total of 2239 patients underwent total thyroidectomy during the period between January 2003 and December 2011 in the Department of Otolaryngology in Venizeleio General Hospital of Heraklion Crete, Greece. The medical records of all patients with a final pathologic report of papillary thyroid carcinoma were reviewed retrospectively.

All patients included in the study underwent standard total thyroidectomy. Surgical management of the patients was recommended upon referral to our hospital for heterogeneous reasons, such as malignant or suspicious thyroid nodules by FNAB, multinodular goiter, hyperthyroidism, or compression of neighboring structures. All patients were operated on by the same surgeons, and the histopathological evaluation of thyroid specimens was performed by three pathologists at our institution. The entire gland and additional nodal tissue were evaluated from 1-mm-thick anatomical slices. Patients who had metastasis detected preoperatively by FNAB, or intraoperatively by palpation of the central neck compartment, underwent a level VI therapeutic dissection as described in the American Thyroid Association 2009 guidelines.

Inclusion criteria in our study were adult age, standard total thyroidectomy, preoperative ultrasound (U/S) diagnosis of dominant nodule located in the thyroid isthmus and histopathological diagnosis of papillary thyroid carcinoma. Exclusion criteria were previous neck surgery, family history of cancer and history of neck radiation.

Of all total thyroidectomy patients ($n = 2239$), 122 patients (5.45%) had a dominant thyroid nodule in the isthmus. Patients with nodules of the isthmus were divided into two main groups based on the results of the histopathological examination; Group 1, comprised patients ($n = 68$) with benign dominant thyroid nodule of the isthmus, and Group 2, comprised patients ($n = 54$) with papillary thyroid carcinoma in dominant nodule of the isthmus.

From all total thyroidectomy patients, 634 (28.3%) presented malignant neoplasms, of which 575 patients had papillary carcinoma diagnosed by histopathological examination. In 54 patients (9.1%), PTC was located to a dominant nodule of the isthmus. This group of patients with isthmic PTC was sub-divided into two groups based on the size of the lesion; Group A, comprised patients ($n = 27$) with PTC >10 mm and group B, comprised patients ($n = 27$) with microcarcinoma (PTMC) ≤10 mm), according to the World Health Organization criteria [16].

The clinical characteristics considered for statistical analysis were age (≤45 years versus ≥45 years), gender (male versus female), weight of thyroid gland (≤30 g vs >30 g) and clinically cervical lymph node metastases at the time of diagnosis (cN0 versus cN+). The histopathological characteristics considered for statistical analysis were size of the tumor at its greatest diameter (≤10 mm versus >10 mm), histological subtype (pure papillary, follicular, sclerosing, tall cell variant), histopathological evidence of autoimmune thyroid disease, focality of tumor (solitary isthmus nodule vs multifocality vs bilaterality). The 7th edition of the American Joint Committee on cancer (AJCC), TNM classification of malignant tumors in 2010 was used to describe and categorize cancer stages and progression.

Multifocal disease was defined as more than one tumor focus in thyroid parenchyma. The tumor focus with the largest diameter (dominant nodule) was considered as the primary carcinoma. Bilateral disease was defined as tumor foci located in both thyroid lobes.

Univariate analysis was performed with the Pearson Chi-square test and Fisher Exact test as appropriate. A p value <0.05 was considered statistically significant. SPSS software (SPSS 17. Inc. Chicago, IL) was used for statistical analysis.

3. Results

Of the 2188 total thyroidectomy patients, 575 had papillary carcinoma diagnosed by histopathological examination. Dominant thyroid nodules of the isthmus presented totally 122 patients, of whom 68 patients (Group 1) had benign nodules and 54 (Group 2) had malignant nodules. Among the isthmic dominant nodule patients, 95 were female and 27 male, with a male/female ratio of 1/3.5. Mean age of these patients at surgery was 51.26 ± 13.53 years. Eighty one patients (66.4%) were over 45 years of age and 41 (33.6%) under 45 years. Mean nodule diameter was 11.43 ± 8.43 mm. Sixty three patients (51.6%) presented a dominant nodule of the isthmus 10 mm or less and 59 (48.4%) a dominant nodule larger than 10 mm (Table 1). There were no significant differences between the two groups of patients in terms of gender, size of nodule and autoimmune disease. Male patients in Group 1 and Group 2 were 13 (19.1%) and 14 (25.9%) respectively ($p = 0.368$). Mean dominant nodule diameter in Group 1 was 11.06 ± 5.30 and in Group 2 was 12.13 ± 8.81 mm ($p = 0.0747$). In addition, autoimmune thyroid disease was histologically confirmed in 16 patients (23.5%) of Group 1, and 15 patients (27.8%) of Group 2 ($p = 0.592$).

Fifty four patients (Group 2) had a dominant PTC located in the isthmus. These patients represented a 9.2% rate of our total PTC patients. Univariate analysis of these patients showed that age at diagnosis was significantly associated with the malignant isthmic