ORIGINAL ARTICLE

Cancer rate of Bethesda category II thyroid nodules

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ABSTRACT

Aim Thyroid nodules are very common and may be found in more than 50% of the population. Fine-needle aspiration cytology (FNAC) of thyroid nodules is a very useful diagnostic tool with high sensitivity and predictive value for diagnosis. The Bethesda System for Reporting Thyroid Cytopathology (BSRTC) uses six categories for thyroid cytology reporting (I-nondiagnostic, II-benign, III-atypia of undetermined significance (AUS)/ follicular lesion of undetermined significance (FLUS), IV-follicular neoplasm/suspicious for follicular neoplasm (SFN), V-suspicious for malignancy, and VI-malignant. Our objective was to determine the malignancy rate in Bethesda II nodules.

Methods From June 2010 to May 2020 a retrospective analysis was performed among 1166 patients who underwent thyroid surgery for benign thyroid diseases in our institution. Thyroid cytopathological slides and Ultrasound (US) reports were reviewed and classified according to the BSRTC. Data collected included age, gender, cytological features, and histological type of thyroid cancer.

Results During the study period, 44.77% (522/1166) of patients with an FNA categorized as Bethesda II underwent thyroid surgery. Incidental malignancy was found in 1.53% (8/522) cases of Bethesda II. The most common malignant tumour type was papillary thyroid carcinoma.

Conclusion The current study demonstrates that incidental thyroid carcinoma can be diagnosed after thyroidectomy even in patients with an FNA categorized as Bethesda II.

Key words: benign nodule, Bethesda classification, malignancy rate

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INTRODUCTION

According to the National Cancer Institute (NCI), thyroid cancer is the third fastest rising malignancy in the United States (1). Thyroid nodules are very common and may be found in more than 50% of the population. However, the majority of them are benign lesions (2). Fine needle aspiration cytology (FNAC) is the gold standard for the preoperative evaluation of thyroid nodules. Its results constitute the main criteria for selecting patients who are candidates for surgery (3). Indications for FNAC include: lesions bigger than 10mm with high risk characteristics in ultrasound (US) imaging, nodules bigger than 20mm that either exhibit characteristics of intermediate risk for malignancy or that exhibit progressive enlargement, nodules in patients with family history of thyroid cancer, and nodules with a long axis of 5mm that exhibit suspicious US characteristics – hypoecogenicity, increased vascularity, irregular orders or microcalcifications (4). Mean FNA sensitivity and specificity for malignancy are calculated at 83% and 92% respectively, with a mean false-negative rate of 5.2% and a false- positive rate of 2.9% (5).

The Bethesda system for reporting thyroid cytopathology, which constitutes the most widely used reporting system for FNA results, categorizes them into six groups: non-diagnostic or unsatisfactory specimen (I), benign lesion (II), atypia of undetermined significance (AUS) or follicular lesion of undetermined significance (FLUS) (III), follicular neoplasm or suspicious for a follicular neoplasm (IV), suspicious for malignancy (V), and malignant (VI). Lesions yielding Bethesda II results include: nodular goitre, adenomatoid and colloid nodules, Graves' disease, Hashimoto's disease and subacute thyroiditis (6,7).

The aim of this study was to determine the malignancy rate of Bethesda II nodules in patients undergoing thyroidectomy for benign thyroid diseases in the Department of Surgery at the General University Hospital of Patras in Greece.

PATIENTS AND METHODS

Patients and study design

Between June 2010 and May 2020, 1166 patients underwent thyroid surgery for benign thyroid diseases in tertiary General University Hospital in Patras/Greece, covering a population of approximately 1.5 million people. A total of 522 patients had an FNA categorized as Bethesda II, and were considered for this retrospective study.

Methods

Data were collected from medical and operating theatre records as well as from the Hospital-coded database including patient characteristics (age at operation, gender), length of hospital stay, operative parameters (time and type), and histological outcome.

Statistical analysis

Student's t-test for normally distributed variables, Mann – Whitney U test for skewed variables, and Fisher's exact tests were used to compare results between groups. A $p<0.05$ was considered statistically significant.

RESULTS

During the study period, 522 (out of 1166; 44.77%) patients with a FNA categorized as Bethesda II underwent thyroid surgery. Of these 522 patients, 514 (98.47%) were diagnosed with benign lesions, whereas eight (1.53%) were diagnosed with thyroid cancer. Total thyroidectomy was performed in 120 (23%) of the nodules with Bethesda II, subtotal thyroidectomy in 402 (77%) of cases.

Females were more frequently represented than males in either malignancy or benign group. The mean age of patients with a benign lesion at the time of surgery was 49.3±12.11years, having no significant difference with the patients with malignancy, which was 48.7±11.37 years. In addition, there was no significant difference regarding operation time, as well as duration of hospital stay (Table 1).

Table 1. Number of cases, gender, age, duration of hospitalization, surgery operative time according to histological outcome of 522 Bethesda II patients

Variable	Histological outcome of Bethesda II patients		p
	Benign	Malignancy	
Number (%) of patients	514 (98.47%)	8 (1.53%)	<0.05
Males/Females (104/418)	102/412	2/6	>0.05
Mean (±SD) age (years)	49.3±12.11	48.7±11.37	>0.05
Duration of hospitalization (±SD) (days)	4.2±2.9	4.1±2.4	>0.05
Mean operative (±SD) time (min)	105.1±57.2	107.3±48.9	>0.05

The most common cancer type in patients diagnosed with malignancy was papillary thyroid carcinoma accounting for five (out of eight; 62.5%) cases. There were two (25%) patients with follicular thyroid carcinoma (FTC), whereas only one (12.5%) was found to have medullary carcinoma.

DISCUSSION

Thyroid nodules have become relatively common in clinical practice, and their prevalence increases with age. The majority of thyroid nodules are benign. However, the risk of malignancy in adults ranges from 5% to 15% (8).

The results of our study demonstrate 1.53% rate of malignancy for patients with Bethesda category II thyroid nodules, and papillary thyroid carcinoma as the most common subtype. According to the literature, approximately 70% of all FNAs are categorised as Bethesda II, while 3% of these are expected to be false-negatives according to the BSRTC (9). Surgical series report noticed a false negative rate of 8 to 14% (4). Specimen related problems such as inadequate sampling are responsible for the majority of false negative diagnoses, with other contributing factors including low quality slide preparation and lack of experienced cytopathologists and radiologists (9-10). A controversial factor related to false negative results is the size of the nodule undergoing FNA. There are studies that point out that nodules of greater size, especially those bigger than 4cm, are more prone to false positive FNA results, with rates reaching 17%-19%, than their smaller counterparts, missing as many as 13% of cancers and 34% of follicular lesions, whereas others discount this (10-11).

Measures that can be implemented in order to decrease false negative rates include repeated biopsies and the involvement of a cytopathologist. Repeated FNA biopsies have been proven to reduce the false positive rates, especially in nodules with high risk ultrasonographic features (TIRADS 4-5) (4). There is evidence that one repetition of an initially benign biopsy can decrease the false-negative rate from 17% to 11% and increase the sensitivity from 81% to 90%, while further repetitions of the examination have been found offer limited benefit (5). More specifically interpretation of the FNAB examination by a cytopathologist has been linked with a 76-fold decreased risk of false-negative results, consequently a consultation of such an expert is advised (10).

The main limitation of this study is a retrospective assessment from a single centre. In addition, the tumour node metastasis (TNM) staging system was not recorded for malignant tumours (12). Our study indicates the need for a prospective randomized controlled trial of patients with Bethesda category II thyroid nodules in order to include more information such as ultrasound characteristics of the nodules and thyroid nodule size.

In conclusion, the current study demonstrates that incidental thyroid carcinoma can be diagnosed after thyroidectomy even in patients with an FNA categorized as Bethesda II. Repeated FNA biopsies have proven to reduce the false negative rates in this category of patients.

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TRANSPARENCY DECLARATION

Conflict of interests: None to declare.

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