Acta Biomed 2022; Vol. 93, N. 6: e2022288 DOI: 10.23750/abm.v93i6.13528

Original article

Thyroid carcinoma in nodules with Thy3 cytology: retrospective study in a district general hospital

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Abstract. *Background and Aim:* Thyroid cancer is the most common malignant endocrine tumour. Fine needle aspiration cytology plays an important role in diagnosis of these tumours. The aim of the current study was to determine thyroid cancer risk for Thy3 cytology over a seven-year period from 2015 to 2021 at Royal Lancaster Infirmary, UK. *Methods:* 206 medical records with Thy3 cytology were retrospectively reviewed from January 2015 to December 2021. Patients were classified into two groups: Thy3a and Thy3f. Histopathology reports were compared with cytology reports in order to determine malignancy rates. *Results:* 18.9% of male patients and 23% of female patients had a malignant histology The average overall malignancy rate was 22.2%. More specifically, 22% of Thy3a and 22.4% of Thy3f were malignant. 22 patients eventually underwent completion thyroidectomy of which 6 patients had malignancy in the contralateral lobe. *Conclusion:* Malignancy rates at our center was lower as compared to the national data rates.

Key words: thyroid, thyroid cancer, FNAC, Thy3 cytology, hemithyroidectomy

Introduction

The most common endocrine malignant tumour is thyroid cancer, but this constitutes less than 1% of all cancers treated in the United Kingdom (1). There has been a steady rise in the number of thyroid cancers being diagnosed but the overall mortality has remained unchanged over the past many years (2). Distinguishing benign from malignant thyroid cancers is not always easy. Fine needle aspiration cytology (FNAC) as well as ultrasound play a crucial role in the diagnosis of thyroid swellings. All patients with suspected thyroid cancer should undergo a thyroid ultrasound (3).

In the United Kingdom, FNAC is reported according to the Thy system described by the royal college of pathologist (2). Thy3 cytology suggest the possibility of neoplasm and is further classified into Thy3a for cellular atypia and Thy3f for follicular neoplasm. The malignancy rates are 5-15% and 15-30% for Thy3a and Thy3f, respectively (2). In order to confirm malignancy in these cases histopathology is required to look for capsular and angioinvasion which confirms malignancy (4). Based on British Thyroid Association (BTA) 2014 guidelines (3), Thy3f cytology should undergo diagnostic hemithyroidectomy while Thy3a needs ultrasound assessment with or without a repeat FNAC.

The aim of the current study was to determine thyroid cancer risk for Thy3 cytology over a seven-year period from 2015 to 2021 at Royal Lancaster Infirmary.

Patients and methods

This is a retrospective observational study where all Thy3 cytology reports and corresponding histology reports were reviewed from January 2015 to December 2021at Royal Lancaster Infirmary, UK. All reports were obtained from online pathology database.

Demographic data was collected for all patients. Only Thy3 nodules that had histology and preoperative

ultrasound reports available were included in the study. Exclusion criteria included paucity of information regarding histology, ultrasound and FNAC. All Thy3 reports were further divided into two groups which are Thy3a and Thy3f.

Statistical analysis was performed on Microsoft Excel. Histopathology reports were compared with FNAC reports in order to determine rate of malignancy associated with Thy3 cytology. Since there was no direct patient interaction informed consent was not needed and waiver of consent was sought with ethical committee.

Results

In the current study, 206 medical records were reviewed from January 2015 to December 2021. 4 patients were excluded due to missing data in patient electronic records leaving behind 202 patients for the study. All patients were further classified into two groups i.e., Thy3a and Thy3f. Total number of patients in Thy3a were 59 (29.2%) and Thy3f were 143 (70.8%) (Table 1).

Age of patients ranged from 27-95 years and 22-93 years in Thy3a and Thy3f and average age of patients in years with a malignant histology was 60 in both Thy3a and Thy3f. There were more female patients in the study (81.6%) with average malignant histology in females being 23% and in males being 18.9% (Table 1).

Out of the 59 cases found to be Thy3a, 46 patients had a benign histology and 13 were malignant. Eight out of the 13 malignant cases met criteria for a completion thyroidectomy. Out of the eight cases that underwent completion thyroidectomy 3 were found to have malignancy in the contralateral lobe. There were 143 cases classified as Thy3f cytology of which 111 were benign and 32 had malignant histology. 14 out of these 32 cases underwent completion thyroidectomy of which 11 were benign and three were malignant (Figure 1). Overall rate of malignancy in our study for Thy3 lesions was 22.2%. The rate of malignancy in the Thy3a patients was 22 % and 22.4% in Thy3f patients.

Histological outcomes following surgery for both the groups have been summarised in Table 2. The most common benign histology in Thy3a group was follicular adenoma (26.1%) followed by Hashimoto's thyroiditis (23.8%) while the most common malignant tumour in Thy3a group was classical variant of papillary thyroid cancer (PTC) (29.4%). The most common benign tumour in the Thy3f group was also follicular adenoma (43.2) and the most common malignant tumour was follicular variant of PTC (25.6%).

Table 3 and Table 4 summarises the ultrasound grading for thy 3 nodules based on U classification of thyroid nodules. Risk of malignancy for U3 or indeterminate ultrasound was 25.6% and 30.6% for Thy3a and Thy3f groups respectively.

Table 1. Demographic Data.

	Thy3a	**Thy3f**
Total number of patients (202)	**59**	**143**
Age (years)		
• Range	27-95	22-93
• Average	60	59.9
Gender		
• Male	9	28
• Females	50	115
• Malignant histology in males	2	5
• Malignant histology in females	11	27

Discussion

The British Thyroid Association (BTA) issued new guidelines for the management for thyroid cancers in 2014 (5). The Royal College of Pathologist UK guidance document (2) classify thyroid cytology into 5 categories ranging from non-diagnostic (Thy1) to confirmed malignant (Thy 5). When it comes to Thy3a cytology, general recommendations by BTA are a repeat ultrasound with or without a repeat FNAC. If a second FNAC shows Thy3a then this requires multidisciplinary team discussion. Thy3f cytology on the other hand should undergo diagnostic hemithyroidectomy as the possible differentials include hyperplastic nodule, follicular adenoma or follicular carcinoma.

Interpreting Thy3 cytology has always been challenging because cytology cannot show vascular or capsular invasion which are hallmark features of malignancy. Malignancy rates with Thy3a and Thy3f cytology are 5-15% and 15 - 30%, respectively (2).

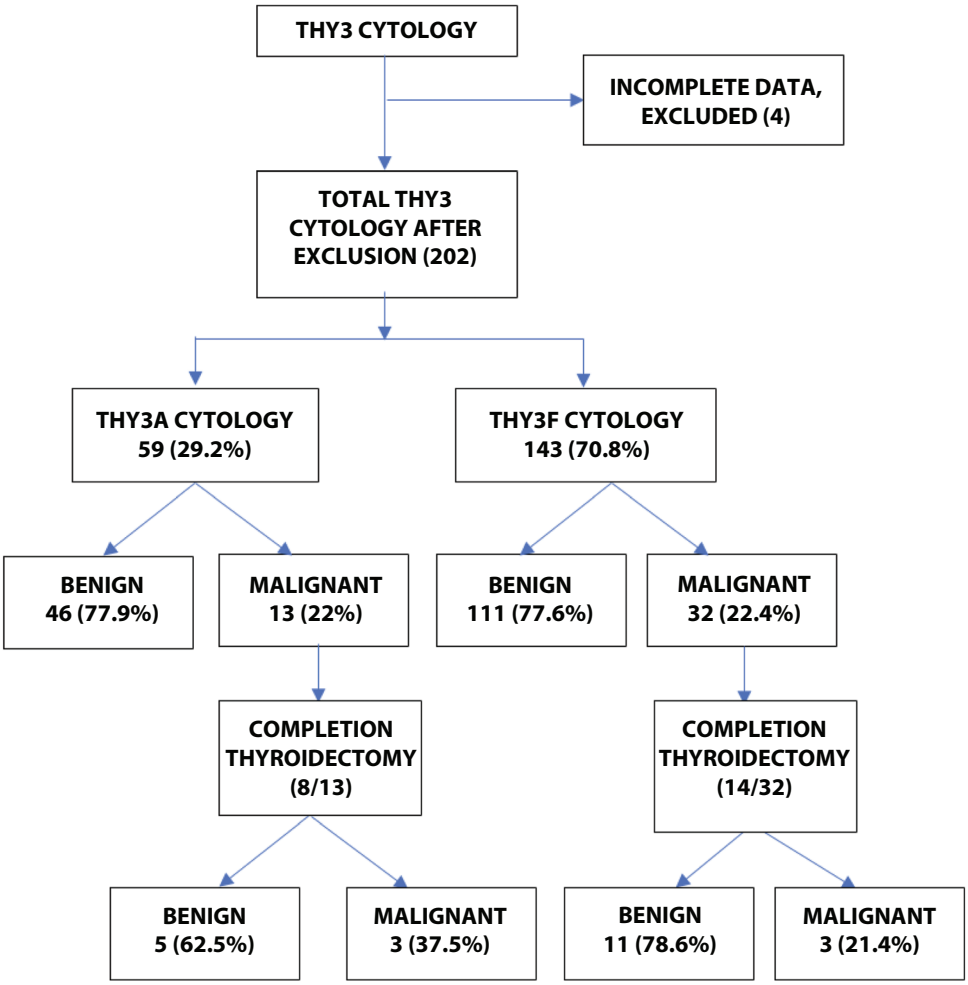

Figure 1. Flow Chart showing outcome of Thy3 nodules.

In the current study, malignancy rate was 22% for Thy3a cytology and 22.4% for Thy3f cytology and an overall average of 22.2% which is lower compared to nationally quoted figure of 27.8% (UK sixth national thyroid audit report, 2021) (6). BTA guidelines (5) states that malignancy rates for Thy3 nodules can vary anywhere from 9.5 to 43%. A study by Nair et al. (7) and Ho et al. (8) reported higher malignancy rates for indeterminate cytology of 40% and 37.8%, respectively while a study by Alexander et al. (9) reported a malignancy rate of 24.7% for Thy3 cytology. This reinforces the fact that malignancy rates are quite variable.

Majority of patient with Thy3 cytology undergo a diagnostic hemithyroidectomy. Hemithyroidectomy is associated with significant morbidity which includes hoarseness of voice (injury to recurrent laryngeal nerve), bleeding and scarring. A benign histology report following a diagnostic hemithyroidectomy requires no further intervention. A finding of malignant histology on the other hand requires further management. This may be in the form of completion thyroidectomy with radioactive thyroid ablation. The size of the tumour and associated risk factors like age, lymph node invasion, angioinvasion and extracapsular spread decide if further intervention is required (5). Studies have shown that tumours < 4cms in size and no risk factors, hemithyroidectomy alone has equally favourable outcome to total thyroidectomy (10,11). In our study, a total of 22 patients underwent completion

Table 2. Histological outcome following surgery.

	Thy3a	Thy3f
Benign (total)	**46**	**111**
Colloid Nodule	4	7
Multinodular Goitre	4	17
Hashimoto's thyroiditis	10	10
Granulomatous thyroiditis	1	0
Adenomatoid Nodule	9	15
Follicular adenoma	11	45
Hurtle cell Adenoma	3	10
Encapsulated follicular pattern thyroid tumours		
• NIFTP	4	6
• WDT-UMP	0	1
Malignant (total)	13	32
Classical PTC	5	4
Follicular variant, PTC	2	10
Microcarcinoma, PTC	2	8
Hobnail Type, PTC	1	0
Oncocytic, PTC	0	1
Spindle cell Variant, PTC	1	0
Follicular thyroid cancer (FTC)	2	4
Minimally invasive, FTC	0	2
MTC	0	1
Hurtle cell Carcinoma	0	2

Table 3. Ultrasound Grading of Thy3a nodules based on U classification.

U Classification	Number of Patients	Benign histology	Malignant histology
U2	14	14	0
U3	39	29	10
U4	4	2	2
U5	2	1	1

Table 4. Ultrasound Grading of Thy3f nodules based on U classification.

U Classification	Number of Patients	Benign histology	Malignant histology
U2	50	44	6
U3	75	52	23
U4	15	13	2
U5	3	2	1

thyroidectomy of which 6 patients had malignancy in the contralateral lobe.

There also a subset of thyroid tumours that sit between benign and malignant and these include minimally invasive follicular thyroid cancer and encapsulated follicular pattern thyroid tumours such as non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) and well-differentiated tumours of uncertain malignant potential (WDT-UMP). In our study there were 10 cases of NIFTP, 1 case of WDT-UMP and 2 cases of minimally invasive FTC. A retrospective study by Nikiforov et al. (12), found that after a median follow up of 13 years there was no disease recurrence in 67 cases of NIFTP.

The main limitation of the current study is that it is a retrospective study hence only patients with

histological outcome have been included. Majority of the histology and cytology reports have been reported by pathologist with interest in thyroid cytology and this helps in lowering the interobserver variability.

Conclusion

The overall rate of malignancy in our study was 22.2% which was lower that the national average of 27.8%. Malignancy rates can vary from centre to centre, and it would be useful if each centre calculates their individual rate as this information can be shared with patients who can have a better understanding of malignancy rate when it comes to Thy3 cytology.

Conflict of interest: The author declares that he has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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Received: 4 July 2022
Accepted: 4 August 2022
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