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Research Article

Predicting Thyroid Nodule Malignancy Using TI-RADS and U-grading, a Retrospective Sonographical Analysis

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Abstract

Introduction: British and American guidelines both utilise ultrasound (US) to determine the likeliness of a thyroid nodule being malignant based on a criteria of certain sonographic features. Is there a significant difference between grading systems in identifying malignant thyroid nodules?

Methods: A blinded retrospective cohort analysis of 115 thyroid US scans for adult male and female patients who underwent total or hemi thyroidectomy. BTA U and ACR TI-RAD scores were allocated and compared against final histology to assess for correlation. Two independent head and neck radiology physicians ensured inter-observer variability was reduced.

Results: The largest proportion of malignant lesions lie in the U2 category (13.9%) compared to U3 (8.69%) and for TI-RAD, malignant T2 lesions is 2.6%. Under the TI-RAD system a larger proportion of patients are sampled due to most U2 lesions being T3 categorised but malignant pickup is marginally higher at 11.3% vs 8.69% with a 20% increase in the number of patients needing to be sampled. Overall, patients were scored higher using TI-RAD.

Conclusions: When comparing the TI-RAD against the U-grading system, the latter has greater specificity, PPV and NPV. Limitations are U2/T2 (benign) and U3/T3 (indeterminate) graded lesions. TI-RAD grading is radiologically more cautious; therefore, more lesions are sampled for a modest increase in detection. Both systems have positive and negative attributes but the financial and patient morbidity associated with excess investigation the TI-RAD system does not offer a greater pickup rate based on risk but rather volume. Given the current financial burden on the NHS, is implementation of a system which increases clinical and investigation time for an 11% increase in cancer pickup rate beneficial? The rationale behind such a comment is that radiological identification of disease identified varies and one must also consider the importance of false positives and incidentalomas.

Keywords: Thyroid Nodule; Thyroid Cancer; Ultrasound; Risk; Standards

Introduction

Nodules within the thyroid gland display diverse sonographic features and when combined with variability in radiologist interpretation the threshold for fine needle aspiration (FNA) [1] can expose many patients with known or incidental thyroid nodules to further investigations. These come at cost to the health service and also carry a morbidity to the patient. As a result of this over 250 articles have been published which aim to provide guidelines on the management of thyroid nodules over the last decade [2].

British (BTA) and American (TI-RADS) guidelines both utilise ultrasound (US) to assess the probability of malignancy in thyroid nodules greater than 1cm and the likelihood of malignancy is again based on the presence of certain sonographic features which are

graded from 1-5 (the higher the number, the greater the risk stratification). The key difference between both guidelines is that the BTA system gives the highest score based on the single most suspicious feature detected on US. TI-RADS however gives the presence of each adverse feature a numerical value and the cumulative total of these determines the overall score. The higher the total score, the greater the chance of malignancy and need for sampling via FNA [3].

There has been great debate surrounding the implementation of TI-RADS to replace the current BTA 2014 guidelines and this paper aims to compare both guidelines directly in a UK NHS based system to assess accuracy. Literature searches to date show that no studies directly comparing these guidelines has been published. The aim of the information obtained here has the potential to provide further evidence to aid in the decision making towards the management of thyroid nodules on a national level.

Material and Methods

A two-part retrospective single blind analysis of post-operative histology of 115 adult male and female patients over the age of 18 over a three-year period between 2014 and 2017 at our institution (Great Western Hospital) was undertaken. Inclusion criteria were all patients who had undergone a hemi or total thyroidectomy for an FNA confirmed differentiated thyroid cancer, FNA showing Thy 3F or two consecutive Thy3A taken three months apart. These cases subsequently had a retrospective re-analysis of their pre-operative ultrasound images (which had already been U-graded) by the same two head and neck radiologists who were blinded to the post-operative histology to provide a new TI-RADS score.

The second part involved comparison of the FNA cytology against final post-operative histology. This is to calculate sensitivity and specificity of BTA and TI-RADS grading systems and whether this is reflected in cytology. Exclusion criteria included all cases of completion thyroidectomies, total thyroidectomy or any thyroid procedure performed for an indication other than presumed or confirmed malignancy.

All US images used in this analysis were recorded with a Toshiba Aplio MX Ultrasound unit coupled with a Toshiba 12Mhx Linear Array Transducer PLT-12804BT. All FNA taken at the time were performed by the same consultant head and neck radiologist experienced in thyroid imaging via a locally agreed protocol using a 22g needle. A total of 4 samples were always sent with 2 fixed and 2 air dried on glass slides for each patient with use of infiltrative anaesthesia. All FNA which were suggestive of differentiated thyroid cancer were discussed in a dedicated thyroid MDT where imaging and cytology was re-evaluated to further reduce variability.

Results and Analysis

There were 115 suitable cases which were analysed (Table 1). When comparing both grading systems.

For Thy3A nodules 13 cases were identified of which one was malignant and graded as U4/T3 with final histology showing follicular variant papillary carcinoma and given the grading the patient would have undergone FNA using either guideline.

Cancer status at histology	**U Grading score of nodule**				
	U1	U2	U3	U4	U5
Positive	0	16	10	4	6
Negative	1	52	21	4	1
	TI-RADS score of nodule				
	T1	T2	T3	T4	T5
Positive	5	3	13	8	7
Negative	12	8	45	13	0

Table 1: Gross results showing proportion of malignant and non-malignant thyroids at histology and their comparison with ultrasound grading with each guideline.

Thy 3F (38 cases in total)					
BTA	U1	U2	U3	U4	U5
	0	18	14	4	2
TIRADS	T1	T2	T3	T4	T5
	1	3	25	7	2

Table 2: Table showing distribution of Thy 3F nodules based by ultrasound grading with each guideline.

US Grading	**Number**
U2/T2	2
U2/T3	4
U3/T3	4
U3/T4	1
U4/T4	1
U5/T5	2
	14

Table 3: For Thy3F nodules 14 of the 38 cases were found to be malignant on histology and the grading of each guideline they were associated with.

Statistic	Value	95% CI
Sensitivity	38.46%	20.23% to 59.43%
Specificity	91.23 %	80.70% to 97.09%
Positive Predictive Value	66.67% (*)	43.17% to 84.04%
Negative Predictive Value	76.47 % (*)	70.36% to 81.65%

Table 4: Analysis of U grading system for obtained data values.

Statistic	Value	95% CI
Sensitivity	65.22%	42.73% to 83.62%
Specificity	60.61 %	42.14% to 77.09%
Positive Predictive Value	53.57% (*)	40.74% to 65.95%
Negative Predictive Value	71.43 % (*)	57.27% to 82.34%

Table 5: Analysis of TI-RAD grading system for obtained data values.

Discussion

The U grading system alone as a predictor of malignancy is unreliable and must be used in conjunction with FNAC [4-8]. When compared to the TI-RAD grading system it appears that the U grading system has greater specificity and is a stronger PPV and NPV. The limitations to both systems are when faced with U3 and T3 graded lesions which are indeterminate and therefore require further investigation [9]. In this study, when using TI-RAD scoring, a larger proportion of patients which were U2 would be upgraded into a T3 category and undergo FNAC however the number of positively malignant nodules is unaffected.

TI-RADS investigates a larger cohort of patients with thyroid nodules with no subsequent increase in the number of positively malignant nodules identified but rather an overall larger number of benign nodules confirmed with cytology which is reflected in table 1 there the largest cohort of patients which were U2 become T3 with negative histology for malignancy.

As a diagnostic tool for risk stratifications, both grading systems require the use of FNAC to increase positive predictive value [10]. When directly comparing the TI-RADS grading system against the U grading system, it appears that the U-grading system has greater specificity and stronger PPV and NPV. As the system relies on identifying the single most suspicious feature, the absence of any would strongly suggest the absence of malignancy and this is reflected in the specificity. The lower sensitivity reflects in the requirement for FNAC when suspicious features are found to help confirm the presence or absence of malignancy.

The converse is true for TIRADS as the scoring is based on a cumulation of risk defining features and the greater the number of sonographic features the more likely a lesion is to be suspicious. This is why sensitivity is higher at 65.22% compared to 38.46% for U-grading. The specificity is lower however as in the TIRADS scoring system it is easier to upscale a lesion to a higher scoring category so exclusion based on lack of features is less likely whereas U-grading is more basic in this respect.

Limitations to both systems are when faced with U2/T2 (benign) and U3/T3 (indeterminate) graded lesions. 13.9% of U2 lesions are found to be malignant and this is in keeping with the national average of between 9-13%. One does not overtly appear to be superior compared to the other in this study overall.

When considering the TI-RAD grading system, a larger proportion of lesions which would be U2 would be upgraded to a T3 when using TI and therefore warrant FNAC. This would yield a greater proportion of morbidity and expense for the health system with the trade that more patients with disease would in theory not be 'missed'. The TI-RAD system has a 2.6% incidence of malignancy of T2 nodules.

Conclusion

Based on our study, it appears that both systems have positive and negative attributes but ultimately given the financial and patient morbidity associated with excess investigation. The TI-RAD system does not offer a greater pickup rate based on risk but rather volume. The authors suggestion based on the work carried out is that given the current financial burden on the NHS, implementation of a system which increases clinical and investigation time for an 11% increase in cancer pickup.

Statistically this increase sounds extremely beneficial however we must consider how many patients require ultrasound scanning in order to positively identify one positive nodule using the TI-RAD system. Another consideration is to the histology and severity of disease picked up; these can be extremely variable and one must also consider the importance of false positives and radiologist variability [11] when investigating such a large volume of patients.

A multi-center single blinded pre-implementation trial of the TI-RAD grading system against the current U-grading system would allow for controlled monitoring of pre and post-operative outcome measures. This type of study design would allow for the number of patients seen to be carefully monitored and direct comparison of

scan, FNA and post-operative histology along with clinical efficacy to be monitored. The additional benefit of a multi-center approach is to allow for a real time assessment of whether current facilities and setup would allow for the new grading system to be implemented efficiently with minimized disruption should the outcomes be favorable towards using the TI-RAD system [12].

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