The appropriateness of ultrasound imaging for thyroid pathology, the standard of radiology reporting on thyroid nodules and the detection rates of thyroid malignancy: A tertiary centre retrospective audit.

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Abstract for: **The appropriateness of ultrasound imaging for thyroid pathology, the standard of radiology reporting on thyroid nodules and the detection rates of thyroid malignancy: A tertiary centre retrospective audit.**

OBJECTIVE: To determine the number of inappropriate requests for thyroid ultrasound (US), the quality of radiology reporting for thyroid nodules based on accepted guidelines and the resultant number of thyroid cancers identified because of these investigations.

MATERIALS AND METHODS: Electronic medical records of patients who underwent thyroid US imaging and thereafter referred to the Endocrine Department at Gold Coast University Hospital, QLD between July 2014 and July 2017 were reviewed. Data for 251 patients who had thyroid US performed and the final 201 patients who were found to have thyroid nodules were evaluated using descriptive statistics. Indications for thyroid US imaging amongst referring clinicians were assessed and we compared both clinical and radiology reporting practises of thyroid nodules to the published 2009 and 2015 American Thyroid Association(ATA) guidelines.

RESULTS: There were 50.2% of patients with initial thyroid US imaging deemed outside of expert recommendations where 42% of these patients required further surveillance imaging and 25.4% required fine needle aspiration of their thyroid nodules. A definite recommendation whether to further evaluate thyroid nodules were provided in 44.8% of radiology reports. There were no radiology reports that described thyroid nodules findings based on patterns as recommended by the 2015 ATA guidelines. Two cases of thyroid cancer were detected including one patient with prior history of thyroid cancer and a second patient with hypothyroidism.

CONCLUSION: Routine use of US thyroid imaging outside expert recommendation is common. There is lack of standardised reporting when assessing thyroid nodules on US. Limiting the initial use of US in cases of palpable neck lumps and the use of systematic reporting according to the 2017 guidelines published by the American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS) may reduce unnecessary investigations for thyroid nodules in the future.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/imj.14401

INTRODUCTION:

The use of ultrasound (US) imaging in assessing thyroid pathology should be selective. Over-use of US has been previously reported for indications outside expert recommendations.¹

US imaging should not routinely be used in cases of thyroid dysfunction. In specific cases, such as in amiodarone induced thyrotoxicosis, US imaging of the thyroid gland with flow-Doppler may assist in assessing the type of thyrotoxicosis.^{2,3} US imaging of the thyroid gland should generally be in the context of assessing thyroid nodule(s) following identification of a palpable neck lump(s), surveillance of a previously suspicious thyroid nodule, surveillance for thyroid cancer recurrence following thyroidectomy in conjunction with assessment of thyroglobulin and thyroglobulin antibodies as well as for characterising a thyroid nodule when incidentally detected through other imaging modalities. The Royal Australasian College of Physicians and the Endocrine Society of Australia have recently discouraged the use of US in the investigation of thyroid function abnormalities in the absence of a palpable thyroid abnormality (<https://evolve.edu.au/published-lists/esa/>).

The purpose of US imaging of thyroid nodules is to distinguish between low-risk, benign nodules from higher-risk nodules which are potentially malignant. The latter may require serial US imaging and or fine needle aspiration (FNA). The 2015 American Thyroid Association (ATA) and more recently the 2017 American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS) have issued guidelines on the standards of thyroid US reporting which would help guide further management of these nodules. US imaging should look at features including thyroid nodule size, location, presence of pathological appearing lymph nodes, nodule echogenicity, nodule margins, presence and type of nodule calcification as well as shape and vascularity status of the nodule.⁴ Suboptimal reporting which includes insufficient information on the characteristics of a thyroid nodule identified on ultrasound imaging could result in unnecessary follow up and intervention.

To determine the frequency of such problems, we conducted a retrospective audit to determine the appropriateness of thyroid US scans performed and to assess the quality of the radiology report as well as the number of thyroid cancers being diagnosed because of these investigations in patients referred to the Gold Coast University Hospital.

MATERIALS AND METHODS:

This study is a single-centre retrospective chart audit of adult patients who were referred to the endocrine department with thyroid nodules between the periods of July 2014 to July 2017. This period of study was chosen to investigate most recent referrals and clinical practise. The study is conducted during the time where there is overlap of the 2009 and 2015 ATA guidelines on the management of thyroid nodules. The department of endocrinology has a large referral base with Gold Coast University Hospital and Health Service overseeing a catchment area of more than 590,000 people. A list of patients who were referred with thyroid nodules for the period studied were obtained from the booking and referrals centre which keep electronic records of all patients referred to the outpatient department.

Data was then collected from all available resources where most data was readily available from the referral letter scanned into our Electronic Medical Record (EMR) system. Other sources of data collection included Queensland Pathology, private pathology services, Gold Coast University Hospital

radiology department as well as the reports from other local radiology units within the catchment area.

Data collected included indications for US imaging, initial thyroid function tests results, size of largest thyroid nodule, whether concerning features of detected thyroid nodules were reported by radiologists (hypo-echoic, taller rather than wide, micro-calcifications or rim calcifications, peri-thyroidal or abnormal cervical lymph nodes, solid nodule measuring $>1\text{cm}$, mixed solid-cystic nodule $\geq 1.5\text{cm}$, presence of intra-nodular vascularity, and the presence of irregular, spiculated nodular margins or extra-capsular invasion), radiologists and endocrinologist recommendations, whether serial US imaging was performed and the number of serial US imaging performed during the study period, change in nodule characteristics following serial US imaging and whether comparison was made with prior findings, result and number of FNAs performed, whether patients were referred to surgeons and pathology results following thyroidectomy.

Thyroid ultrasound was regarded as appropriate if done to investigate a palpable thyroid nodule or neck mass, to follow-up a previously identified thyroid nodule and in those regarded as high-risk such as those exposed to ionising radiation. Hypothyroidism, hyperthyroidism or the presence of neck pain without a palpable nodule were regarded as inappropriate indications.

Data collection was done in a password protected excel file accessible to only those involved in the study. Data was analysed using descriptive statistics. Results are shown as number (%) or mean $\pm$ standard deviation.

Ethics approval was obtained through the Gold Coast Health Service Human Research Ethics Committee (LNR/2018/QGC/49220).

RESULTS:

A total of 361 patients were audited during the study period (see **Figure 1**). We excluded 109 patients who did not meet the inclusion criteria. Data for 251 patients were analysed, where data for 51 patients who had no thyroid nodules were included in the assessment for inappropriate US imaging and data for the remaining 201 patients with thyroid nodules were further evaluated for nodule characteristics, follow-up management and outcomes.

Figure 1: Selection and exclusion of subjects for audit.

General practitioners accounted for 171 of the 201 referrals (85.1%) followed by 29 internal hospital referrals from various specialists (14.4%) and 1 private specialist referral (0.5%). Most patients with thyroid nodules were females (85.6%) (51.5 ± 14.7 years) compared to males (14.4%) (58.6 ± 15.9 years). **Figure 2** shows the clinical indications for US imaging.

Figure 2: Clinical indications for thyroid ultrasound.

There were 126/251 (50.2%) initial thyroid US scans performed prior to referral to the endocrine department which were deemed outside of expert recommendations where 50/126 (39.7%) were for hyperthyroidism 58/126 (46%) were for hypothyroidism including one case of positive TPO with no thyroid dysfunction and 18/126 (14.3%) were for neck pain without a palpable mass. As a consequence of the initial non-clinically indicated US scans, 53/126 (42%) patients had further serial imaging performed on nodules deemed suspicious by either the radiologist or endocrinologist and 32/126 (25.4%) underwent FNA with a resultant diagnosis of thyroid cancer found in only 1/126 (0.79%) patients.

Of the 201 patients who had thyroid nodules on imaging report, the radiologist provided a definite recommendation whether to further evaluate these nodules through FNA or US imaging, or no further evaluation required in 90 cases (44.8%). In the remaining 108 (53.7%) US imaging reports, the treating endocrinologist made the decision whether to follow up the nodules based on the descriptive findings mentioned on the radiology report.

We found 69/201 reports which did not mention any concerning features other than size of the nodule(s). There were 3/201 US reports which were unavailable for review. For thyroid nodules measuring ≤ 1.5 cm with no concerning features, endocrinologists recommended follow up in 6/46 (13%) cases and radiologists recommended follow up in 9/46 (19.6%) cases. We found only 3 US imaging reports which mentioned detection of lymph nodes with no documentation whether these

lymph nodes were normal or abnormal in appearance. One of these patients had a known prior history of thyroid cancer.

Figure 3 shows concordance in recommendations for follow-up between radiologist and clinician in those cases where the radiologist provided a definite recommendation.

Figure 3: Comparison between radiologist and endocrinologist decision whether to further investigate thyroid nodules.

Of the 201 patients, 114 (56.7%) proceeded to serial US imaging and 103 (51.2%) had FNA performed. Results for 99/103 patients who had FNAs done were available for assessment (7 Bethesda 1, 71 Bethesda 2, 10 Bethesda 3, 8 Bethesda 4, 1 Bethesda 5 and 2 Bethesda 6). Three patients declined or had an unsuccessful attempt and the result for one patient was unavailable for review.

There were 20/201 (9.9%) patients who were referred for surgical resection with a final thyroid cancer diagnosis seen in 2/201 (0.99%) patients. (see **Table 1**) One patient was already known to have thyroid cancer and suffered a recurrence and one patient had hypothyroidism with incidental finding of a thyroid nodule measuring 1.1-1.5cm. (see **Table 2**)

Serial US imaging was performed in the same centre for 65 patients, where 84.5% of the reports compared their findings to the previous scan results. In 8 patients, no comparison was made with the original scan. Serial US imaging was performed in a different centre for 49 patients where only 19 reports were compared with previous scans.

Indications for thyroid US	Number of patients with thyroid nodules	Number of patients with thyroid cancer

Coincidental finding on imaging for another reason	32	0
Compressive symptoms	7	0
Following monitoring of known thyroid nodules	28	0
Hyperthyroidism	37	0
Hypothyroidism	35	1
Neck pain with no palpable neck lump	16	0
Palpable neck lump	39	0
Thyroid cancer surveillance	5	1
Unclear reason not mentioned above	1	0
TPO antibody positive with nil abnormal TFTs	1	0
Total number of patients =	201	2

Table 1: Indications for US imaging of the thyroid gland and diagnosis of thyroid cancer.

FNA results	Nodule size	Number of concerning features	Histology results	Reason surgery not performed if referred for resection
Bethesda 1	>1.5cm	1	Benign	
Bethesda 1	>1.5cm	>1		Failed to attend follow up
Bethesda 1	>1.5cm	1		Opted for serial US imaging
Bethesda 3	>1.5cm	1	Benign	
Bethesda 3	>1.5cm	1	Benign	
Bethesda 3	>1.5cm	1	Benign	
Bethesda 3	>1.5cm	1	Benign	
Bethesda 3	>1.5cm	1	Benign	
Bethesda 3	>1.5cm	0	Benign	
Bethesda 3	</= 1cm	>1		Declined surgery
Bethesda 4	>1.5cm	1	Benign	
Bethesda 4	>1.5cm	1	Benign	

Bethesda 4	>1.5cm	1	Benign	
Bethesda 4	1.1-1.5cm	1	Benign	
Bethesda 4	1.1-1.5cm	>1	Benign	
Bethesda 4	>1.5cm	1		Followed up privately- data unavailable
Bethesda 4	1.1-1.5cm	0		Followed up privately- data unavailable
Bethesda 5	1.1-1.5cm	0	Benign	
Bethesda 6	1.1-1.5cm	0	Papillary thyroid cancer	
Bethesda 6	-	1	Papillary thyroid cancer	

Table 2: Histology results following referral for thyroidectomy.

DISCUSSION:

Within the published literature, thyroid nodules are found in 30-60% of autopsy studies.⁵ In the living population, incidental thyroid nodules are found in up to 70% of patients undergoing a neck ultrasound for various indications.^{6, 7} Thyroid nodules are common in areas of iodine deficiency. Pre-adulthood exposure to ionising radiation is a known risk factor for developing thyroid nodules and thyroid cancer. Familial tumours may account for 5-15% of thyroid cancer cases.⁸ Hashimoto's thyroiditis is also associated with increased risk of thyroid nodules. Most thyroid nodules are benign. When thyroid incidentalomas are detected on positron emission tomography (PET) scanning, the probability of malignancy is around 35%.⁹ This study included one patient with an FDG avid thyroid nodule on PET scan, which measured less than 1cm on US imaging, which was followed with US after discussion with patient and considering their co-morbidities.

There are many studies showing a worldwide rise in the incidence of thyroid cancer especially for the papillary thyroid cancer subtype without a corresponding increase in mortality.^{10, 11} Many studies attribute the rise or over-diagnosis of thyroid cancer to the use of more sensitive imaging.^{12, 13, 14} This however is not consistent worldwide. In the United States, from 1994 to 2013, the incidence of thyroid cancer diagnosis increased partly due to increased utilisation of imaging modalities which detected small localised cancers, but there was also an actual increase in incidence of advanced papillary thyroid cancers potentially attributed to environmental factors.¹⁵ The population thyroid cancer mortality rate was shown to increase albeit much less than the incidence rate.¹⁵ Similarly, in Queensland, Australia, the incidence of well-differentiated thyroid cancer has increased significantly over the last 30 years independent of socio-economic groups and for both early and advanced disease.¹⁶ Again, it was postulated that over-diagnosis through imaging may not account for all the observed thyroid cancer incidence and that there may be other factors such as obesity, the decline in smoking, and the exposure to radiation from increased use of diagnostic imaging particularly in children which may account for the real rise in thyroid cancer incidence.¹⁶ Overall these studies show that there is a rise in the incidence of both clinically significant and non-clinically significant thyroid cancers where the rise of non-clinically significant thyroid cancers are likely a result of the increasing use of diagnostic imaging.^{15, 16}

Our study revealed that 50.2% of US imaging performed at initial referral to the endocrine department was not indicated. A total of 126 scans were performed for the clinical indication of hyperthyroidism, hypothyroidism and neck pain. Importantly, neck pain is a rare presentation for thyroid cancer and therefore US imaging in this instance should not be routine.¹⁷ The recently published Queensland Thyroid Cancer Study further confirmed that the probability of diagnosing lowest risk papillary thyroid micro-carcinomas was related to US imaging of benign thyroid disease including cases of hypothyroidism, hyperthyroidism, monitoring of thyroid nodules which were noted on other imaging modalities and the use of US imaging for assessing the thyroid gland after surgery for a benign thyroid condition.¹⁸

There were only 2 patients in our study who were diagnosed with thyroid cancer. The first patient was someone who already had a prior history of thyroid cancer undergoing surveillance imaging. The second patient was someone who had imaging done for hypothyroidism. The scan picked up a thyroid incidentaloma measuring 1.1-1.5cm with no concerning features however the radiologist recommended FNA and the cytology results confirmed malignancy. Surgery was subsequently performed and histology results confirmed a diagnosis of papillary carcinoma. It is arguable that the patient would not have had a clinically significant cancer if the nodule was not further investigated. We also considered whether there were suspicious findings not described on the report as the radiologist recommended FNA follow up. This audit showed that the yield of diagnosing thyroid cancer after inappropriate indications for initial US imaging is low (0.79%). Half of such patients required surveillance imaging and a quarter required assessments through FNA studies. The flow-on effects following inappropriate initial imaging of the thyroid gland need to be considered. Although not specifically assessed, the need for multiple clinic reviews, surveillance imaging and interventions contribute to our rising economic health-care burden. These patients are also likely subjected to unnecessary anxiety during their investigative journey for the reassurance of a benign cause.

The ATA have developed and revised guidelines over the years to help direct management of thyroid nodules and differentiated thyroid cancer. Our audit would have overlapped the interval where the 2009 ATA guidelines for management of thyroid nodules were already established and a period of 18months when the revised 2015 ATA guidelines were published in January 2016.

The 2009 ATA guidelines provided strong recommendations to perform FNA on anyone with abnormal cervical lymph nodes on imaging and in patients with thyroid nodules measuring >5mm with suspicious US imaging findings if the patient had a high-risk history including history of thyroid cancer in one or more first degree relatives, history of external beam radiation as a child, pre-adulthood exposure to ionising radiation, prior hemi-thyroidectomy with discovery of thyroid cancer, ¹⁸FDG avidity on PET scanning, and history of multiple endocrine neoplasia or familial medullary thyroid cancer. (see **Table 3**)

In 2015, the ATA updated and revised the earlier guidelines which were then published in January 2016. Thyroid nodules are now classified into 5 different patterns from highly suspicious to benign patterns. A more conservative approach was employed where FNA was recommended for the highly and intermediate suspicious thyroid nodules if the size was ≥ 1 cm. If the nodule was of low suspicion pattern, FNA is only recommended if the size was ≥ 1.5 cm. (see **Table 3**)

<i>Sonographic pattern</i>	<i>US features</i>	<i>Estimated risk of malignancy, %</i>	<i>FNA size cutoff (largest dimension)</i>
High suspicion	Solid hypoechoic nodule or solid hypoechoic component of a partially cystic nodule with one or more of the following features: irregular margins (infiltrative, microlobulated), microcalcifications, taller than wide shape, rim calcifications with small extrusive soft tissue component, evidence of ETE	>70–90 ^a	Recommend FNA at ≥ 1 cm
Intermediate suspicion	Hypoechoic solid nodule with smooth margins without microcalcifications, ETE, or taller than wide shape	10–20	Recommend FNA at ≥ 1 cm
Low suspicion	Isoechoic or hyperechoic solid nodule, or partially cystic nodule with eccentric solid areas, without microcalcification, irregular margin or ETE, or taller than wide shape.	5–10	Recommend FNA at ≥ 1.5 cm
Very low suspicion	Spongiform or partially cystic nodules without any of the sonographic features described in low, intermediate, or high suspicion patterns	<3	Consider FNA at ≥ 2 cm Observation without FNA is also a reasonable option
Benign	Purely cystic nodules (no solid component)	<1	No biopsy ^b

US-guided FNA is recommended for cervical lymph nodes that are sonographically suspicious for thyroid cancer (see Table 7).

^aThe estimate is derived from high volume centers, the overall risk of malignancy may be lower given the interobserver variability in sonography.

^bAspiration of the cyst may be considered for symptomatic or cosmetic drainage.

ETE, extrathyroidal extension.

Table 3: Adapted from Revised American Thyroid Association Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer by Haugen et al. Thyroid. Vol 26, No.1, 2016. Copyright permission granted by Mary Ann Liebert, Inc., New Rochelle, NY.

Before and after the publication of new guidelines, decision making on further investigation was regularly made by the clinician. In the absence of detailed US findings, it is likely this decision making was based on nodule size and other factors identified in the history. There may also be different expectations between clinicians and radiologist as to whose responsibility it is to provide recommendations for follow up.

It is unclear why follow up was recommended by endocrinologists or radiologists in the cohort of patients with thyroid nodules measuring <1.5cm with no concerning features. We did not scrutinise individual patient records for historical indicators of higher risk which may have contributed towards need for further follow up. Patient anxiety may have also affected decision making.

The fact that there were no radiology reports that described thyroid nodule findings based on patterns as recommended by 2015 ATA guidelines after 18 months of publication may reflect delayed change in practise by radiologists. It is likely only those radiologists highly involved in thyroid US may follow endocrine literature, further explaining slow uptake of reporting recommendations. Lack of only 3 reports commented on lymph nodes.

There was better comparison reporting for serial scans when the scan is performed in the same centre as the initial scan compared to when it is performed elsewhere. This is not surprising given the easier access to prior imaging reports when the scan is performed in the same centre.

The most recent 2017 guidelines published by the American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS) may influence reporting in the coming years. This guideline outlines a risk stratification system to identify most clinically significant thyroid malignancies while reducing the number of biopsies performed on benign nodules. This guideline also provides recommendation for interval US imaging. Using this method of reporting, thyroid nodules are assessed for 5 characteristics including composition, echogenicity, shape, margin and

echogenic foci.¹⁹ All abnormal neck lymph nodes would require biopsy.¹⁹ Thereafter thyroid nodules are classified into 5 different TI-RADS (TR) categories from TR1 (benign) to TR 5 (highly suspicious).¹⁷

Depending on the TR category, either FNA or US may be recommended. In comparison to the 2015 ATA guidelines, nodules that are deemed low suspicion should only be biopsied if the size is >2.5cm and those which are moderately suspicious should be biopsied if the thyroid nodule measures > 1.5cm.¹⁹ The aim was not to diagnose every potential malignant thyroid nodule, rather to focus on thyroid nodules that would be clinically significant. The higher cut-offs were chosen as the ACR TI-RADS group perceived that the cumulative risk for distant metastasis from papillary and follicular cancer based on the graph published by Machens et al., occurred more gradually at a size larger than 2cm and because Machens et al., studied surgical specimens rather than US dimensions, where US imaging tend to report larger sizes compared to pathologic sizing.²⁰ The ACR TI-RADS committee decided against the pattern based approach used in the 2015 ATA guidelines following a study by Yoon et al., which showed that there were 3.4% of 1293 nodules that were not classifiable and out of these 18.2% were found to be malignant.²¹ The committee also recommended against scanning intervals of less than one year unless the patient has proven thyroid cancer under active surveillance.¹⁹ It was thought that the recommended interval and total time of surveillance imaging would decrease the likelihood of significant malignancies remaining undetected over time and would be in keeping with the trend towards active surveillance for low-risk thyroid cancer.¹⁹

The Endocrinology Department at the Gold Coast University Hospital discourages the use of US in patients with thyroid dysfunction alone, providing the information on the electronic template, however many patients with thyroid dysfunction have US examinations. In reality, it would be difficult to avoid inappropriate requests for US imaging as most requests are done at a primary care level. Increasing the awareness amongst primary care clinicians is important through published articles, guidelines through the Royal Australian College of General Practitioners and educational talks within local health services are recommended. If inappropriate indications for US imaging is found in bigger studies within Australia consideration to remove the Medicare benefit item for US imaging requests for hyper- and hypothyroidism unless requested by an endocrinologist could be considered. We propose this as a consideration given a similar situation in the past where there was inappropriate testosterone prescribing; and following limitations placed on prescribing this drug, the subsequent number of patients initiating testosterone therapy markedly decreased.²²

This study has limitations. The study sample is of note where it included only patients who were referred to the endocrine department. Anecdotal information suggests patients referred to a surgeon were mostly likely to have a FNA or US finding highly suggestive of cancer. It would have been valuable to assess whether these patients had appropriate initial indications for US imaging. There may be a significant amount of US imaging requests performed within primary care services which are not referred to hospital specialists which would have likely added to the number of inappropriate scan requests. The additional numbers would have strengthen the study in assessing current US imaging indications and practices amongst general practitioners and hospital specialists.

SUMMARY:

The routine use of US thyroid imaging for indications outside of expert recommendations is common. There is lack of standardised reporting of thyroid US examinations. Limiting thyroid US to the assessment of neck masses and palpable thyroid abnormalities and the systematic reporting of

thyroid US according to the TI-RADS system is likely to result in a reduction of unnecessary investigations.

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