The utility of thyroid ultrasonography in the management of thyroid nodules

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Background: Ultrasonography for thyroid nodules is one of the most common imaging tests performed in the general population. Details from ultrasound reports guide biopsies and surgery. This study quantifies the completeness of these reports based on Thyroid Imaging and Reporting System (TI-RADS) criteria and considers their utility in predicting malignant disease.

Methods: We retrospectively reviewed ultrasound reports for 329 thyroidectomy patients and extracted data elements using the TI-RADS criteria: nodule size, echogenicity, margins, vascularity, solid/cystic composition and the presence or absence of microcalcifications and the halo sign. We assessed the reports to determine whether individual or multiple criteria were associated with malignancy.

Results: More than 97% of reports document nodule size; however, more than 90% of the reports noted only 3 or fewer of the 6 remaining TI-RADS criteria. The presence of microcalcifications was the most sensitive marker of malignancy (> 90%), whereas the documentation of irregular margins was the most specific indicator of malignancy (88%). Overall it was clear that microcalcifications, hypoechogenicity, irregular margins and solid nodules were significantly more likely to be found in malignant neoplasms; their absence predicted benign disease. Because so few reports consistently documented all criteria, the overall ability of thyroid ultrasonography to discriminate between lower- and higher-risk nodules is limited.

Conclusion: Although the accuracy of thyroid ultrasonography is good, few ultrasound reports contain the necessary information, as defined by TI-RADS, to predict malignancy and guide management. When reported, microcalcifications and/or irregular margins are the best predictors of malignancy.

Contexte : L'échographie des nodules thyroïdiens est l'une des épreuves d'imagerie les plus souvent effectuées dans la population générale. Les détails fournis par l'échographie guident les biopsies et la chirurgie. Cette étude quantifie l'exhaustivité des rapports d'échographie selon les critères TI-RADS (Thyroid Imaging and Reporting System) et en mesure l'utilité pour prédire les cancers.

Méthodes : Nous avons passé en revue de façon rétrospective les rapports d'échographie de 329 patients ayant subi une thyroïdectomie et nous en avons extrait les éléments sous l'angle des critères TI-RADS : taille des nodules, échogénicité, marges, vascularité, composition solide c. kystique, présence ou absence de microcalcifications et signe du halo. Nous avons évalué les rapports afin de déterminer si certains critères individuels ou multiples pouvaient être associés au cancer.

Résultats : Plus de 97 % des rapports mentionnent la taille des nodules; mais, plus de 90 % des rapports ne font état que de 3 critères ou moins sur les 6 autres critères TI-RADS. La présence de microcalcifications a été le marqueur tumoral le plus sensible (> 90 %), tandis que la présence de marges irrégulières a été le marqueur tumoral le plus spécifique (88 %). Dans l'ensemble, les microcalcifications, l'hypoéchogénicité, les marges irrégulières et les nodules solides ont sans contredit été significativement plus susceptibles d'être observés en présence de malignité; et en revanche, leur absence permettait de prédire une maladie bénigne. Étant donné que si peu de rapports ont documenté avec constance tous les critères, la capacité globale de l'échographie de la thyroïde à distinguer entre nodules de risque faible et élevé est limitée.

Conclusion : Même si la précision de l'échographie thyroïdienne est bonne, peu de rapports d'échographie renferment les renseignements nécessaires, selon les critères TI-RADS, pour prédire un cancer et orienter sa prise en charge. Lorsqu'elles sont signalées, les microcalcifications ou les marges irrégulières sont les meilleurs prédicteurs de cancer.

The increasing prevalence of thyroid nodules presents an important challenge to physicians who treat thyroid cancer.¹⁻³ Palpation, the traditional means to identify thyroid nodules has been supplanted by ultrasonography; some studies have shown that more than half of all ultrasounds reveal nodular disease.^{4,5} More than 90% of all nodules represent benign disease, but because most nodules persist and rarely regress completely, the pre-eminent question facing physicians is how to use ultrasonography to identify and treat thyroid nodules.^{4,6} More than 30 studies in the last year alone have examined the utility of thyroid nodule ultrasonography to predict malignancy based on different features.^{4,7-10} In a recent meta-analysis, Brito and colleagues¹¹ documented substantial heterogeneity across studies; the typical reporting schemes for thyroid ultrasounds are unclear, as is the practical utility of using ultrasounds to perform risk stratification of thyroid nodules.¹¹

The Thyroid Imaging and Reporting System (TI-RADS) was developed to provide a minimum common data set for standardized risk stratification of thyroid nodules.^{7,12-15} For a thyroid ultrasound report to conform to TI-RADS it must include the following nodule characteristics: marked hypoechogenicity, taller-than-wide shape, microcalcifications, irregular margins and solid component in addition to size.^{2,15-17} First used by Horvath and colleagues,¹⁴ the TI-RADS system is analogous to the standardization of breast imaging by which categories defining risk of malignancy are used as part of the synoptic reporting scheme for assessments.¹⁵ In a recent prospective study, mirroring the results of previous retrospective analyses, the risk of thyroid malignancy was found to be 0% in TI-RADS categories 1 and 2, 0.64% in category 3, 4.76% in category 4A, 66.67% in category 4B, 83.33% in category 4C and 100% in category 5.⁸ Since this initial work, the process has become generally accepted, with the American College of Radiology further defining the appropriate vocabulary. The European Thyroid Association (ETA), American Thyroid Association (ATA) and the American Association of Endocrinologists (AAE) endorse the use of ultrasonography to stratify nodules into low, intermediate, and high risk of malignancy.¹³

The reality facing many physicians is that the reporting of thyroid ultrasounds originates from multiple sites and is dictated by physicians of varying experience, practice volumes and styles of documentation.^{9,18-20} There is very little research on the content of the actual ultrasound reports that radiologists provide to physicians. Thus, the value of ultrasound reports, regardless of whether they have used the TI-RADS reporting scheme or not, remains unclear. In a cohort of patients from a single endocrine surgery referral centre that treats both benign and malignant thyroid disease, we assessed the completeness of ultrasound reports against the TI-RADS criteria and then correlated the ultrasound findings with the final pathology.

METHODS

We performed a retrospective study comprising patients from a single surgical referral centre (at the University of Alberta) who had been assessed for thyroid surgery between January 2009 and December 2013. Permission to conduct this study was granted by the Health Research Ethics Board of Alberta (ethics approval #HREBA.CC-16-0359). We included patients who met the following criteria: they were assessed only for thyroid nodular pathology, had an ultrasound report within 18 months of referral, did not have previous neck or thyroid surgery, were older than 18 years, and underwent surgery that allowed for pathologic confirmation of the index nodule assessed by ultrasonography. We excluded patients in whom the ultrasound failed to detect a discrete lesion that was sonographically discernible; patients in whom no ultrasound was completed, or whose ultrasound report was dated more than 12 months before surgery; patients with a family history of thyroid cancer, as defined by 2 or more first-degree relatives; patients exposed to high-dose radiation either inadvertently or as part of medical treatment; and patients with subsequent pathology results revealing lymphoma.

Patients with complete ultrasound reports and final pathology were then included in the review, in which we assessed each report for inclusion of nodule size, macro- or microcalcifications, echogenicity, margins, halo sign, vascularity, and solid or cystic components. For the purposes of this study, a thyroid nodule was defined as a discrete lesion sonographically distinguishable from surrounding parenchyma. Internal components were recorded only if there was an explicit report of solid, cystic, or mixed components, and final analysis was carried out for any nodule with an explicit report of "solid" structure. Hypoechogenicity was recorded only if it was specifically noted or if a direct comparison was made to surrounding parenchyma or strap muscle. Microcalcifications were included if reported and/or if distinguished from macrocalcifications. Internal vascularity, halo sign or absence of a halo, and irregular margins were recorded only if it was specifically reported to be either present or absent. Size was always recorded.

Statistical analysis

Statistical analyses were performed using the 2-tailed Student *t* test for unpaired samples, with equal variance. We assessed the correlations using the Fisher exact test for tables and Spearman rank correlation for continuous variables. Statistical tests were 2-tailed, and we considered results to be significant at $p < 0.05$. We used descriptive statistics to present the study variables. Means and standard deviations are reported for the continuous variables, and frequencies and percentages are reported for categorical variables. We calculated likelihood ratios in view of the prevalence of disease, as defined histologically in our cohort or as defined theoretically based on

the literature. We computed the following measures of test accuracy for each variable along with 95% confidence intervals (CIs): sensitivity, specificity, positive likelihood ratio and negative likelihood ratio. All statistical analyses were conducted using SPSS software version 15.

RESULTS

In total, 455 patients had been assessed for thyroid surgery during the study period. Of these, we excluded 66 patients owing to failure of the ultrasound to detect a discrete lesion that was sonographically discernible, 47 patients in whom no ultrasound was completed or

whose report was dated more than 12 months before surgery, 5 patients with a family history of thyroid cancer, 5 patients who were exposed to high-dose radiation and 3 patients whose subsequent pathology results revealed lymphoma, leaving a final cohort of 329 patients. The demographic and clinical characteristics of the cohort are described in Table 1. As expected, there were significantly more women than men in our cohort, and the mean age of patients was 54 years. The size of the nodules assessed in men was slightly larger than in women, but the difference was not significant ($p = 0.24$). Approximately 42% of the nodules were malignant, and the difference in size between benign and malignant neoplasms was not significant ($p = 0.11$). Approximately 11% of specimens also exhibited incidental microcarcinomas on final pathology. The most common carcinoma was papillary thyroid cancer. Benign disease results were dominated by the pathologic description of multinodular goitre, followed by Hashimoto thyroiditis, follicular adenoma and hyperplasia.

The number of documented variables in the ultrasound reports describing the thyroid nodules was assessed and collated for all of the reports. We used the TI-RADS criteria to show what a complete ultrasound report should include: nodule size, echogenicity, vascularity, halo, margins and the presence or absence of microcalcifications. We interpreted the absence of any comment regarding individual criteria as not assessed rather than as a negative result. More than 97% of all reports commented on nodule size, but the descriptions of the other 6 criteria were much more varied. Figure 1 shows the number of reported criteria as a function of benign or malignant neoplasms. Nearly 40% of all reports examined included 1 or no criterion beyond a description of size. The overall distribution of reported scoring criteria did not vary significantly between benign and malignant nodules, and fewer than 10% of all reports described 4 or more criteria other than size. In terms of individually reported criteria, the percentage of reports with a comment was as follows: solid or cystic (51.8%), echogenicity (50.8%), vascularity (31.6%), microcalcifications (28.1%), irregular margins (14.7%), and halo sign (4.5%). There were no associations among the different reporting criteria. We checked for linkages, postulating that the presence of microcalcifications, for example, may trigger more detailed analysis regarding margins or other ultrasound features; however, we did not identify any associations ($p = 0.22$). In addition, neither patient age (< 45 yr v. > 45 yr, $p = 0.29$) nor sex ($p = 0.45$) correlated with the number of ultrasound features reported.

Using the variables reported, we assessed the correlation between the presence or absence of the 6 TI-RADS criteria and malignancy in the index lesion. As shown in Table 2, the presence of microcalcifications was noted in approximately 20% of reports, and the percentage of those reports correlating with malignancy was 31% compared with a

Table 1. Demographic and clinical characteristics of the study cohort

Characteristic	Mean $\pm$ SD, or no. (%)
Age, yr	
Women ($n = 274$)	54.2 $\pm$ 14.0
Men ($n = 55$)	51.3 $\pm$ 14.02
Tumour size at diagnosis, cm	
Women	2.77 $\pm$ 1.58
Men	3.05 $\pm$ 1.74
Primary tumour size, cm	
Benign ($n = 189$)	2.87 $\pm$ 1.65
Malignant ($n = 140$)	2.51 $\pm$ 1.55
Histological diagnosis (index nodule)	
Hyperplasia	15 (4.5)
Follicular adenoma	23 (6.9)
Multinodular goitre	119 (35.7)
Hashimoto	24 (7.2)
Hurthle cell adenoma	8 (2.4)
Follicular thyroid cancer	6 (1.8)
Papillary thyroid cancer	134 (40.2)
Incidental carcinomas	37 (11.1)
SD = standard deviation.

Fig. 1. Number of reported Thyroid Imaging and Reporting System (TI-RADS) criteria as a function of benign or malignant neoplasms.

correlation of approximately 14% with benign neoplasms ($p = 0.044$). Similarly the description of a hypoechoic nodule ($p = 0.005$) or a solid nodule ($p = 0.004$) was significantly more likely to be identified in malignant neoplasms than in benign tumours. Interestingly the documentation of irregular margins demonstrated by far the highest discrepancy, more than 8-fold greater in malignant neoplasms than in benign disease ($p = 0.021$). Descriptions of vascularity ($p = 0.44$) and the presence or absence of a halo ($p = 0.99$) around the nodule were not linked to benign or malignant neoplasms pathologically. It is important to note that a significant proportion of benign nodules exhibited features concerning for malignancy, including microcalcifications and hypoechogenicity, both of which were identified in 1 of every 7 benign nodules. In addition, the percentage of malignant specimens was 32% for nodules less than 2 cm and 28% for nodules greater than 2 cm. The number of reporting criteria did not vary based on nodule size ($p = 0.27$).

Based on the prevalence of malignancy in this cohort, we defined the sensitivity and specificity of the individual ultrasound features and their likelihood ratios (whether positive or negative) in relation to predicting or ruling out malignant disease. The results are outlined in Table 3. The presence of microcalcifications was the single most sensitive predictor of malignancy at just over 90%, with a positive likelihood ratio of 1.6 and a negative likelihood ratio of 0.2. The most specific indicator for a malignancy was irregular margins, with a positive likelihood ratio of 3.1 but a substantially larger CI (Table 3). The other criteria varied in sensitivity and specificity between 24% and 81% and typically exhibited broad CIs below and above 1. As most reports noted 1–3 features, we examined the utility of multiple ultrasound features to predict malignancy. For reports documenting 2 features,

either microcalcifications and hypoechogenicity or microcalcifications and irregular margins in a single nodule, the positive likelihood ratios were 5.2 and 1.7, respectively. Considering the number of reported features as a predictive measure, we found that reports containing at least 3 criteria yielded a positive likelihood ratio of 1.1 and a negative likelihood ratio of 0.9. Thus, the number of features reported did not reflect an increased risk of malignancy. Adjusting for prevalence between 0.5%, 5% and 50% did not substantially alter the likelihood ratios for the analysis. Although we intended to use the data to assess the reports as a function of the TI-RADS scoring system, so few reports documented 4 or more criteria that this was not possible. However, our calculated sensitivity and specificity values for the reported criteria are similar to those reported in the literature, including the study by Brito and colleagues,¹¹ indicating that the TI-RADS scheme likely would be useful in risk stratification in low- and high-volume Canadian centres.^{3,11,21} Of note, we examined the geographical location (urban v. rural centres) of ultrasound reporting; there was no difference in the number of criteria reported ($p = 0.58$), nor were there significant variations in the sensitivity or specificity for individual ultrasound features.

DISCUSSION

In the present assessment of ultrasound reports for thyroid nodules we found that the typical report comments on size and 1 or 2 other criteria, such as echogenicity and solidity. Less than 30% of reports comment on 2 or more criteria beyond size. The number of reported criteria was not linked to the presence of malignant or benign neoplasms. The most common features reported (just over 50%) were

Table 2. Correlation between ultrasound features and malignancy in the index lesion

Ultrasound feature	Overall positive, %	Benign lesion, %	Malignant lesion, %	<i>p</i> value
Microcalcifications	20.5	14.2	30.7	0.044
Hypoechoic	20.1	14.6	32.9	0.005
Irregular margins	5.6	1.8	14.7	0.021
Intranodular vascularity	23.3	21.9	26.1	0.44
Halo sign	2.9	3.2	1.1	0.99
Primarily solid	34.0	28.8	46.6	0.004

Table 3. Sensitivity and specificity of ultrasound features and their likelihood ratios in relation to predicting or ruling out malignant disease

Ultrasound feature	Sensitivity, %	Specificity, %	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Microcalcifications	90.4	43.0	1.6 (1.2–2.1)	0.2 (0.1–0.6)
Hypoechoic	62.5	72.6	2.2 (1.8–2.8)	0.5 (0.4–0.7)
Irregular margins	36.8	87.5	3.1 (1.7–5.7)	0.7 (0.5–1.0)
Intranodular vascularity	77.7	24.2	1.0 (0.9–1.2)	0.9 (0.6–1.4)
Halo sign	46.0	42.8	0.8 (0.6–1.1)	1.2 (1.0–1.5)
Primarily solid	81.1	45.6	1.5 (1.3–1.7)	0.4 (0.3–0.7)

CI = confidence interval.

echogenicity and solidity. There were no associations among reporting criteria; for example, the presence of microcalcifications did not trigger targeted comments about any other factor. This was true for all of the criteria. Malignant neoplasms were more likely to exhibit microcalcifications, hypoechogenicity and irregular margins, and they were more likely to be primarily solid; however, a substantial fraction of benign tumours (14–29%) exhibited similar features. Consequently, the sensitivity and specificity of individual criteria were limited. Microcalcifications were the most sensitive marker of malignancy (90%); irregular margins were the most specific marker (88%). It should be noted that the interpretation of microcalcifications on images can be confused with the presence of echogenic foci secondary to colloid, and this may have decreased the specificity.²² No marker had both sensitivity and specificity exceeding 63%, and consequently the positive likelihood ratio varied between 0.8 and approximately 3.0 in the presence of individual markers. Of the reports that included any 2 criteria, including microcalcifications, echogenicity, irregular margins or solidity, the combined positive likelihood ratio increased to 5.2. To our knowledge, no study has previously investigated the reporting criteria of ultrasounds in a nonspecialized setting or assessed their predictive value as a means to guide management of thyroid nodules. The typical ultrasound report provides limited information beyond the size of the nodule. However, the reported sensitivity and specificity values in our study correlate with those reported in the literature, with microcalcifications and irregular margins representing the most sensitive and specific tests available for stratifying malignant risk.^{23–26}

The TI-RADS scoring criteria were developed to help address the challenge of stratifying the risk of malignancy in thyroid nodules, which are prevalent in up to 60% of the general population.^{3,12,13} The most recent studies examining TI-RADS, both prospectively and retrospectively, allow for a clear distinction between malignant and benign nodules in the vast majority of cases when all scoring criteria are applied.^{8,10,11,15} Kwak and colleagues¹⁵ used a simplified reporting scheme that required reporting the presence of the following criteria: solid component, hypoechogenicity, microlobulated or irregular margins, microcalcifications, and taller-than-wide shape. The benefit of this reporting scheme as opposed to earlier versions of TI-RADS was that it required fewer technical assessments than the original 12 criteria.¹⁴ In fact, even the presence of any 2 factors of microcalcifications, hypoechogenicity, solidity, or irregular margins in the TI-RADS scoring system increases the risk of malignancy to 20%–50%, depending on the study. Conversely, the absence of these findings indicates that the risk of malignancy is 2% or less.^{8,10,11,15} We observed that the calculated sensitivity and specificity values obtained as a measure of the accuracy of ultrasound assessment were also consistent with the literature.

We believe that the TI-RADS system is applicable to our population, and the accuracy of ultrasound reports that

include all the criteria is sufficient to predict the rate of malignancy.^{14,17,25,27,28} The proper application of this system would benefit most from the use of standardized synoptic reporting tools that have been embraced by the surgical community as well as pathologists. In varied settings, including thyroid cancer and pancreatic cancer, synoptic reporting has been examined by international studies and validated as a method for capturing clinical data and improving patient outcomes.^{29–31} Technological advances have made ultrasonography more accessible, and surgeon-directed assessments are now significantly more likely to drive interventions.^{32,33} In fact, the lack of standardized reporting is driving the increased uptake of ultrasonography among surgeons owing to the varied quality of reports, and this trend is accelerating.³³ Ultimately, the combined utilization of synoptic reports with a standardized data system such as TI-RADS could better target those individuals suitable for fine-needle aspiration biopsies and ultimately surgical intervention. This could minimize the current anxiety around thyroid carcinoma and create a more cost-effective assessment pathway for thyroid nodular disease.

Limitations

In applying our findings there are some limitations to consider. The most significant factor may be the disproportionately high malignancy rate in the patient population referred to our centre. This may be a reflection of the fact that patients observed in the community may tend to have smaller tumours, may be older or may lack evidence of other concerning ultrasound features, such as microcalcifications; these patients may not be referred for subsequent investigation and management. Certain patient criteria, such as younger age or smaller nodule size, may also have favoured a more conservative approach that did not include referral for further assessment. However, using varied prevalence rates accepted in the literature for thyroid malignancy in the general population (5%–12%), our likelihood ratios did not change significantly.^{3,4,27} One strength of our study is the inclusion of final pathology, which ultimately has the biggest impact on patient management and outcomes. While individual assessments of sensitivity and specificity could vary, our results are qualitatively similar to those documented in studies that examined individual ultrasound features and the likelihood of malignancy in both urban and rural settings.^{14,17,25,27,28} We acknowledge that there may be differences in the capabilities of individual ultrasonography machines that may limit in some form the reports provided. Finally, this was a retrospective assessment, and over the timeframe of the study there have been upgrades in technology and changes in ultrasonography protocol in different institutions. Despite these changes, ultrasound reports for the most recent 100 thyroid nodule referrals in 2016 still documented only a mean number of reporting features consistent with those observed in our cohort.

CONCLUSION

Although the accuracy of thyroid ultrasonography is good, few ultrasound reports contain the necessary information, as defined by TI-RADS, to predict malignancy and guide management. When reported, microcalcifications and/or irregular margins are the best predictors of malignancy.

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