Benign and Malignant Thyroid Incidentalomas Are Rare in Routine Clinical Practice: A Review of 97,908 Imaging Studies

Abhineet Uppal, Michael G. White, Sapna Nagar, Briseis Aschbrook-Kilfoy, Paul J. Chang, Peter Angelos, Edwin L. Kaplan, and Raymon H. Grogan

Abstract

Purpose: Thyroid nodules incidentally identified on imaging are thought to contribute to the increasing incidence of thyroid cancer. We aim to determine the true rate of incidental thyroid nodule reporting, malignancy rates of these nodules, and to compare these findings with rates of detection by dedicated radiology review.

Methods: A cross-sectional analysis was done to determine the prevalence of thyroid nodules in radiologist reports by analyzing all reports for CT, PET, and MRI scans of the head, neck, and chest as well as neck ultrasounds performed at a tertiary care center from 2007 to 2012. Retrospective chart review was performed on patients with a reported thyroid nodule to determine clinical outcomes of these nodules. Radiology reports were compared with dedicated radiology review of 500 randomly selected CT scans from the study group to determine the difference between clinical reporting and actual prevalence of thyroid nodules.

Results: 97,908 imaging studies met inclusion criteria, and 387 (0.4%) thyroid incidentalomas were identified on radiology report. One hundred and sixty three (42.1%) of these nodules were worked up with fine-needle aspiration, diagnosing 27 thyroid cancers (0.03% of all studies, 7.0% of reported incidentalomas). The prevalence of incidentalomas clinically reported was 142/100,000 CT scans, 638/100,000 MRIs, 358/100,000 PET scans, and 6,594/100,000 ultrasounds. In contrast, review of CT scans screening for thyroid nodules had a prevalence of 10%.

Conclusion: Routine clinical reporting of incidental thyroid nodules is far less common than on dedicated review.

Impact: These data contradict the notion that incidentalomas contribute significantly to rising thyroid cancer rates. Cancer Epidemiol Biomarkers Prev; 24(9): 1–5. ©2015 AACR.

Introduction

The incidence of thyroid cancer in the United States has increased nearly 3-fold between 1975 and 2009 (1). This rise has been noted in population groups spanning a range of ethnicities, localities, and ages leading to an estimated cost burden between $18 and $21 billion dollars in the United States alone (2). Despite these data, the reasons for this rise are unknown. The incidence of thyroid cancer has led to significant speculation regarding the contribution of thyroid incidentalomas to rising thyroid cancer rates with very little data to support any conclusions. We hypothesized published thyroid incidentaloma and incidental thyroid cancer rates overestimate the rate of detection in clinical practice due to reliance on data from dedicated imaging reviews. To examine this, we determined the clinically reported rates of thyroid incidentalomas on CT, PET, MRI, and ultrasound at our tertiary care referral center and compared these with the rates identified by a dedicated radiologist review of a sample of the same imaging studies.

Materials and Methods

Study population

All data were gathered under the supervision of the University of Chicago Institutional Review Board. A database of all radiology reports at our institution, maintained by the University of Chicago Human Imaging Research Office was queried for radiologist reports of imaging studies involving the head or neck and performed on adults. Imaging modalities studied included whole body PET/CT, ultrasound of the neck, as well as CT and MRI of the head, neck, and chest. Imaging studies done for thyroid-specific
conditions were excluded from the study. Using these criteria, we identified 97,908 sequential imaging studies performed from January 1, 2007, to December 31, 2012.

Computer-assisted identification of clinically reported thyroid incidentalomas
To identify thyroid incidentalomas, we first searched for all reports mentioning the phrase "thyroid." From this group, studies performed for known thyroid diseases were then identified by searching for the phrases "thyroiditis," "Hashimoto," "Graves," "thyroid cancer," "thyroid carcinoma," "papillary carcinoma," "medullary carcinoma," "follicular carcinoma," "hyperthyroid," or "hypothyroid" and excluded. Reports containing these phrases were displayed for manual review prior to exclusion. Imaging studies not excluded by this algorithm were then reviewed for thyroid incidentaloma. The criteria used for the selection of thyroid nodules included size and ultrasonographic characteristics on ultrasound, use of fine-needle aspiration (FNA), cytology, operative details and pathology reports. Clinical follow-up, further treatment, and time to follow-up time for patients diagnosed with thyroid carcinomas were also recorded.

Chart and radiology review
Patient charts were reviewed for demographic information, reason for imaging, medical history, thyroid nodule characteristics, including size and radiologist’s description, nodule characteristics on ultrasound, use of fine-needle aspiration (FNA), cytology, operative details and pathology reports. Clinical follow-up, further treatment, and time to follow-up-time for patients diagnosed with thyroid carcinomas were also recorded.

In addition, a dedicated blinded retrospective review of 500 randomly selected CT scans from our study cohort was conducted by an expert attending radiologist at our institution. The incidentaloma rates identified from the clinical radiology reports were then compared with dedicated expert radiologist review of a random sample of the imaging studies previously reviewed by text search algorithm.

Statistical analysis
Statistical analyses were performed using Stata 13. Detection rates and sizes between imaging modalities were compared using Student’s t test. Power analysis was performed to determine the sample size of CT studies required for expert radiologist review. Trends of imaging studies performed and incidentalomas reported per year were fit using linear regression analysis. A Fisher exact test was performed to determine statistically significant differences in incidentaloma detection (α = 0.05).

Results
Demographics, incidentaloma, and incidental cancer detection rates
During the study period, 104,708 imaging studies involving the head or neck were performed on adults at the University of Chicago Medical Center (Chicago, IL). Of the 104,708 studies, 6,800 were performed on patients with known thyroid pathology. The majority of excluded patients were removed for a known thyroid malignancy or nodule (89.2%). The remaining 97,908 studies were then screened for thyroid incidentaloma. The computer screening algorithm identified 387 (0.40%) radiology reports of thyroid incidentalomas in the study population. The mean age of patients with an identified thyroid incidentaloma was 59.2 ± 14.4 years; 310 (80%) patients were female. Thyroid incidentalomas were detected in imaging studies performed for a variety of symptoms or conditions (Table 1).

<table>
<thead>
<tr>
<th>Indications for imaging leading to detection of thyroid incidentaloma</th>
<th>Number (Prevalence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperparathyroidism</td>
<td>193 (49.3%)</td>
</tr>
<tr>
<td>Chest/back/shoulder/head/neck pain</td>
<td>47 (11.6%)</td>
</tr>
<tr>
<td>Cancer staging (non-thyroid)</td>
<td>45 (11.6%)</td>
</tr>
<tr>
<td>Cough, SOB, benign lung/cardiac Dz</td>
<td>31 (8.0%)</td>
</tr>
<tr>
<td>Syncope, neurologic symptoms</td>
<td>22 (5.7%)</td>
</tr>
<tr>
<td>Head and neck mass</td>
<td>11 (2.8%)</td>
</tr>
<tr>
<td>Vascular studies</td>
<td>4 (1.0%)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>2 (0.5%)</td>
</tr>
<tr>
<td>Endometriosis</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Subglottic stenosis</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Sarcoid</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Pelvic neuroma</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Pancytopenia</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Papiloma</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Cushing disease</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Not recorded</td>
<td>25 (6.5%)</td>
</tr>
</tbody>
</table>

The imaging modalities detecting thyroid incidentalomas were CT (115, 30%), MRI (37, 10%), PET (28, 7%), and ultrasound (207, 53%). The prevalence of thyroid incidentalomas detected by modality was 142 in every 100,000 CT scans, 638 in every 100,000 MRI scans, 358 in every 100,000 PET scans, and 6,594 in every 100,000 ultrasounds. Rates of reporting of incidentaloma were lowest for CT (0.1%, P < 0.01) and highest for ultrasound (6.6%, P < 0.01; Table 2). The rates of incidental malignancies in reported nodules were 10 in every 100,000 CT scan, 52 in every 100,000 MRI scans, 51 in every 100,000 PET scans, and 382 in every 100,000 ultrasounds. Cancer prevalence was lower for CT (0.01%, P < 0.01) and higher for ultrasound (0.38%, P < 0.01) compared with all other modalities. The rate of cancer diagnosis per nodule did not differ between modalities (Table 2). During the study period the total number of studies performed annually did not increase over time (P = 0.68), nor did the number of CT scans (P = 0.42). The rates of MRI, PET, and ultrasound, however, increased annually in a linear manner during the study period. There were 98% more MRIs, 40% more PET scans, and 128% more ultrasounds performed in 2012 compared with 2007 (P < 0.01 for MRI, PET, and ultrasound). The number of incidentalomas did not demonstrate a linear annual increase (P = 0.98; Fig. 1).

Follow-up of clinically detected incidentalomas
Of 387 incidentalomas, 207 were discovered initially on ultrasound, 180 were diagnosed on cross-sectional imaging and would require follow-up ultrasound per American Thyroid Association (ATA) guidelines (15). The majority, 175 (97%) of these nodules underwent a subsequent ultrasound workup. Follow-up data were not available for the other 5 nodules. From these 382 nodules evaluated by ultrasound, 163 (42.7%) underwent FNA during their evaluation. One-hundred and one (26.4%) nodules were less than 1 cm in size and would not warrant FNA given their low malignant potential. Forty-three (42.6%) nodules went straight to surgical resection. In total, 75 (19.6%) nodules were greater than 1 cm and did not have tissue sampling. The average size of all incidental nodules was 1.7 ± 0.8 cm, 18 (24.0%) were heterogeneous, 16 (21.3%) were hypoechoic, 7 (9.3%) were cystic, 7 (9.3%) were solid, 6 (8.0%) were isoechoic, 2 (2.7%) had calcifications, and the remaining 19 (25.3%) were nonspecific.
Nodules evaluated by FNA were staged per the Bethesda criteria. There were 20 nodules categorized as Bethesda I. Of these, 3 (15%) were resected; one underwent thyroidectomy for metastatic head and neck squamous cell carcinoma which revealed an incidental papillary thyroid cancer, another elected to undergo resection given her history of head and neck radiation and multiple nodules, and a third underwent resection as part of her parathyroidectomy. Eight (40%) of 20 Bethesda I nodules were followed clinically or with ultrasound, 5 (25%) were lost to follow up, and 4 (20%) had persistent Bethesda I cytology on repeat FNA. Of 109 Bethesda II nodules, 3 were resected; one for obstructive symptoms and two for concern for cancer in a 3.3 cm nodule and another in a 4 cm nodule. In total 11 nodules had Bethesda III cytology, 4 (36.4%) were resected per ATA guidelines while 3 (27.3%) patients elected to be followed with ultrasound, 3 (27.3%) were lost to follow up, and one (9.1%) had a negative repeat FNA. Twelve nodules were classified as Bethesda IV cytology, 10 of these nodules were resected per ATA guidelines. Resection was deferred for two nodules given the comorbidities (mesothelioma and breast cancer) of the patients. Of the 6 nodules classified as Bethesda V cytology, 5 of the nodules were resected. The single patient that did not undergo a resection in the Bethesda V group elected for nonoperative management after surgical consultation. Six nodules were classified as Bethesda VI cytology, 5 of these nodules were treated per ATA guidelines with resection and one patient’s nodule was diagnosed as head and neck squamous cell carcinoma metastasis of non-thyroid origin. This patient went on to receive systemic therapy (Table 3).

Twenty-seven (6.9%) image-detected incidentalomas were ultimately diagnosed as a malignancy. Of these 27 cytologically diagnosed cancers, 25 (93%) were resected as described above. On pathology review, the average size of incidental thyroid cancers was 1.2 cm ± 1.4 cm. Seven (28%) of the 25 resected lesions were multifocal. Two formal lymph node dissections were performed, a left modified radical neck dissection yielding 4 of 12 positive nodes and a level 6 paratracheal dissection yielding 4 benign lymph nodes. Median follow-up of thyroid carcinomas was 2.5 years, with nodal recurrence requiring lymphadenectomy in one patient (3.7%). Four patients (15%) were treated with radioactive iodine, all with p13 papillary thyroid cancer. There were no thyroid cancer–related mortalities, however, one patient treated with an incidentally diagnosed thyroid cancer died during this follow-up period of an unrelated cause.

Radiologist review
An attending radiologist at our institution conducted a blinded retrospective review of 500 randomly selected CT scans specifically looking for thyroid nodules. This dedicated review identified 50 incidental thyroid nodules (10%). None of these nodules had been reported in the clinical radiology reports (P < 0.01). These nodules ranged in size from 0.5 cm to 2.2 cm with a mean size of 0.9 cm ± 0.4 cm.

Discussion
Our study is the first to comprehensively examine the clinical reporting, workup, and treatment of reported thyroid incidentalomas across multiple imaging modalities within the same population. Thyroid incidentalomas were clinically reported at a significantly lower rate than that noted on dedicated radiology review. This confirms our hypothesis that the thyroid incidentaloma rate in clinical practice is significantly lower than what is shown in previous studies that use dedicated radiology review.

While the true prevalence of clinically reported incidentalomas at our institution was substantially lower than those reported in the literature, dedicated review of 500 CT exams from our study group demonstrated the true rate of thyroid nodules to be 10%. This rate on dedicated review is similar to previously published rates of 6% to 18% noted on dedicated radiology review (6). This suggests that previous extrapolations of incidentaloma rates based on dedicated review greatly overestimate the rate of thyroid incidentalomas reported in daily practice. While the true prevalence of thyroid nodules in the population is reflected by previous studies, they do not accurately reflect the significantly lower prevalence of thyroid incidentalomas reported in clinical practice.

Discrepancies between rates of incidental thyroid nodules on dedicated review or ultrasound screening compared with those found in clinical practice have been previously described in a review of both the National Lung Screening Trial, and the Prostate Lung Colorectal and the Ovarian Cancer Screening Trial data (16). In addition, we found the rate of clinically reported thyroid incidentalomas varied greatly based on imaging modality, with neck ultrasounds providing a much higher rate of detection than other cross-sectional imaging methods (Table 2). This is likely due to the fact that the majority of these studies were performed.

Table 2. Comparison of incidental thyroid nodules and cancers by imaging modality

<table>
<thead>
<tr>
<th>Imaging modality</th>
<th>Incidental thyroid nodules</th>
<th>Incidental thyroid cancers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (% total)</td>
<td>n (% per modality)</td>
</tr>
<tr>
<td>CT</td>
<td>81343 (82.9%)</td>
<td>115 (0.1%)</td>
</tr>
<tr>
<td>MRI</td>
<td>5798 (5.9%)</td>
<td>37 (0.6%)</td>
</tr>
<tr>
<td>PET</td>
<td>7828 (8.0%)</td>
<td>28 (0.4%)</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>3139 (3.2%)</td>
<td>207 (6.6%)</td>
</tr>
<tr>
<td>Total</td>
<td>97908</td>
<td>387 (0.4%)</td>
</tr>
</tbody>
</table>

Figure 1. Trends in the total number of scans performed and incidentalomas identified annually by imaging modality at the University of Chicago during the study period. There is no trend in the total number of scans (P = 0.68) or the number of incidentalomas identified (P = 0.42).
Table 3. Incidental thyroid nodule cytology

<table>
<thead>
<tr>
<th>FNA results</th>
<th>n</th>
<th>Resected</th>
<th>Bethesda implied risk</th>
<th>Resected cancers</th>
<th>PTC</th>
<th>HCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bethesda I—nondiagnostic or unsatisfactory</td>
<td>20 (12%)</td>
<td>3 (13%)</td>
<td>1 (5%)</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Bethesda II—benign</td>
<td>109 (67%)</td>
<td>3 (4%)</td>
<td>0%-3%</td>
<td>2 (2%)</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Bethesda III—atypia of undetermined significance or follicular lesion of undetermined significance</td>
<td>11 (6%)</td>
<td>4 (36%)</td>
<td>5%-15%</td>
<td>3 (27%)</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Bethesda IV—follicular neoplasm or suspicious for follicular neoplasm</td>
<td>12 (7%)</td>
<td>10 (83%)</td>
<td>15%-30%</td>
<td>3 (25%)</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Bethesda V—suspicious for malignancy</td>
<td>6 (4%)</td>
<td>5 (83%)</td>
<td>60%-75%</td>
<td>5 (83%)</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Bethesda VI—malignant</td>
<td>6 (4%)</td>
<td>5 (83%)</td>
<td>97%-99%</td>
<td>5 (83%)</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Total with FNA</td>
<td>163</td>
<td>37 (23%)</td>
<td>—</td>
<td>19 (12%)</td>
<td>17</td>
<td>2</td>
</tr>
<tr>
<td>Total without FNA</td>
<td>224</td>
<td>43 (19%)</td>
<td>—</td>
<td>6 (3%)</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>387</td>
<td>80 (21%)</td>
<td>—</td>
<td>25 (6%)</td>
<td>23</td>
<td>2</td>
</tr>
</tbody>
</table>

*Single patient not resected per patient request after meeting with endocrine surgery.

*Single patient not resected after nodule diagnosed as metastatic head and neck squamous cell carcinoma.

Through this work, we described a substantially lower rate of incidentaloma and thyroid cancer detection in clinical practice than reported in previously published dedicated radiology reviews as well as our own dedicated review. In addition, the risk of malignancy was found to be lower in our cohort than what has been previously published. Our data show that in clinical practice the majority of incidental thyroid nodules are not routinely reported. This suggests that thyroid incidentalomas are not a significant contributor to the observed rise of thyroid cancers in the United States. These findings support further investigation into other causes for the rising rate of thyroid cancer in the United States.

Disclosure of Potential Conflicts of Interest

P.J. Chang reports receiving a commercial research grant from Philips and is a consultant/advisory board member for Merge, Lifelmage, and Philips. No potential conflicts of interest were disclosed by the other authors.

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Study supervision: A. Uppal, P. Angelos, R.H. Grogan

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