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

Abhineet Uppal1, Michael G. White1, Sapna Nagar1, Briseis Aschebrook-Kilfoy2, Paul J. Chang3, Peter Angelos1, Edwin L. Kaplan1, and Raymon H. Grogan1

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.

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 (2–4). Despite these data, the reasons for this rise are unknown. The detection of thyroid nodules found on imaging obtained for nonthyroid reasons, termed thyroid incidentalomas, has been proposed as a significant source of the rising incidence of thyroid cancer (5). Reviews of cross-sectional imaging in patients with known nonthyroid cancers or healthy volunteers have demonstrated an incidentaloma prevalence of 6% to 18%, depending on the imaging modality studied (6–14). These data, however, were obtained primarily in studies in which the radiologist reviewed images specifically looking for thyroid nodules. This design may overestimate the prevalence of thyroid nodules that are reported clinically. Because data on thyroid incidentaloma rates are almost exclusively from studies specifically looking for thyroid nodules, little is known about the true clinical detection and reporting rates. This has led to significant speculation regarding the contribution of 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 selected and medical charts reviewed to confirm the finding on the imaging study was incidental and not related to any previously known thyroid disease.

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, 6,808 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).

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 MRIs, 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 MRIs, 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 (0.36%, 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 isoechogenic, 2 (2.7%) had calcifications, and the remaining 19 (25.3%) were nonspecific.

Table 1. Indications for imaging leading to detection of thyroid incidentaloma

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number</th>
<th>Prevalence</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoparathyroidism</td>
<td>193</td>
<td>49.9%</td>
<td></td>
</tr>
<tr>
<td>Chest/back/shoulder/head/neck pain</td>
<td>47</td>
<td>12.1%</td>
<td></td>
</tr>
<tr>
<td>Cancer staging (non-thyroid)</td>
<td>45</td>
<td>11.6%</td>
<td></td>
</tr>
<tr>
<td>Cough, SOB, benign lung/cardiac Dz</td>
<td>31</td>
<td>8.0%</td>
<td></td>
</tr>
<tr>
<td>Syncope, neurologic symptoms</td>
<td>22</td>
<td>5.7%</td>
<td></td>
</tr>
<tr>
<td>Head and neck mass</td>
<td>11</td>
<td>2.8%</td>
<td></td>
</tr>
<tr>
<td>Vascular studies</td>
<td>4</td>
<td>1.0%</td>
<td></td>
</tr>
<tr>
<td>Weight loss</td>
<td>2</td>
<td>0.5%</td>
<td></td>
</tr>
<tr>
<td>Endometriosis</td>
<td>1</td>
<td>0.3%</td>
<td></td>
</tr>
<tr>
<td>Subglottic stenosis</td>
<td>1</td>
<td>0.3%</td>
<td></td>
</tr>
<tr>
<td>Sarcoma</td>
<td>1</td>
<td>0.3%</td>
<td></td>
</tr>
<tr>
<td>Pelvic neuroma</td>
<td>1</td>
<td>0.3%</td>
<td></td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>1</td>
<td>0.3%</td>
<td></td>
</tr>
<tr>
<td>Poag disease</td>
<td>1</td>
<td>0.3%</td>
<td></td>
</tr>
<tr>
<td>Cushing disease</td>
<td>1</td>
<td>0.3%</td>
<td></td>
</tr>
<tr>
<td>Not recorded</td>
<td>25</td>
<td>6.5%</td>
<td></td>
</tr>
</tbody>
</table>
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, while 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 pT3 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>81,143 (82.9%)</td>
<td>115 (0.1%)</td>
</tr>
<tr>
<td>MRI</td>
<td>5,798 (5.9%)</td>
<td>37 (0.6%)</td>
</tr>
<tr>
<td>PET</td>
<td>7,828 (8.0%)</td>
<td>28 (0.4%)</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>3,159 (3.2%)</td>
<td>207 (6.6%)</td>
</tr>
<tr>
<td>Total</td>
<td>97,908</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>—</td>
<td>1 (5%)</td>
<td>0</td>
<td>1</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>0</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 malignancya</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—malignantb</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 (39%)</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>

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

bSingle patient not resected per patient request after meeting with endocrine surgery.

preoperatively for hyperparathyroidism specifically screening for thyroid nodules, further exemplifying the fact that thyroid nodules are often times present but are only clinically reported and clinically relevant when imaging studies are specifically screening for these nodules. This is in contrast to a recent study demonstrating that increasing thyroid cancer rates in South Korea can be attributed to dedicated thyroid screening evaluations (17). As there are no dedicated thyroid cancer screening programs in the United States it is unlikely this low rate of clinical reporting could contribute to the national increase in thyroid cancer diagnoses as significantly as some have postulated.

Retrospective review of cancer registry data has noted that both large and small thyroid cancers have increased in incidence in the United States (3). While another review found no difference in median size between incidentalomas and nodules detected during thyroid evaluation and imaging studies (18). This again suggests the overall increase is not due to only detection of small, clinically undetectable tumors and the rise of papillary thyroid cancers in the United States cannot be fully explained by increased or more sensitive imaging studies.

Regardless of how thyroid nodules are detected, the primary concern once reported is the risk of the nodule being malignant. Reported rates for incidentalomas detected by CT harboring malignancy have been 11% for CT, and up to 50% on PET/CT, though this is biased by the limited sensitivity for biologically less active, more likely benign, nodules (19). In our review, malignancy was identified in only 7.0% of incidentally detected nodules (7.0% on CT, 8.1% of MRI, 14.3% of PET, and 5.8% of ultrasound-detected nodules). This suggests these lesions do have a substantial risk of malignancy, but lower than previously reported.

This study is limited by potential biases due to the single-institution retrospective design. Nodule reporting was dependent on the clinical judgment of our institution’s department of radiology, the variability of which can be seen between years. In addition, as a center caring for a large number of thyroid disorders, the radiologists preparing the reports analyzed may have a greater awareness of the concept of thyroid cancer over diagnoses than a typical national cohort. This could lead to clinical underreporting of thyroid nodules in this study. Another limitation was that 75 patients did not receive an FNA of their incidental nodule greater than 1 cm. We therefore have no cytologic or histologic diagnosis of these nodules. Although the majority of these patients had benign appearing nodules on ultrasound and/or are being followed with close observation, a percentage of these may represent a malignancy not captured in this review.

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, LifeImage, and Philips. No potential conflicts of interest were disclosed by the other authors.

Disclaimer

The content is solely the responsibility of the authors and does not necessarily represent the official views of the NCI or the NIH.

Authors’ Contributions

Conception and design: A. Uppal, S. Nagar, P. Angelos, E.L. Kaplan, R.H. Grogan
Development of methodology: A. Uppal, M.G. White, S. Nagar, P. Angelos, R.H. Grogan
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): A. Uppal, S. Nagar, P.J. Chang, P.J. Chang, R.H. Grogan
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): A. Uppal, M.G. White, S. Nagar, B. Aschebrook-Kilfoy, P.J. Chang, P.J. Chang, R.H. Grogan
Writing, review, and/or revision of the manuscript: A. Uppal, M.G. White, S. Nagar, B. Aschebrook-Kilfoy, P.J. Chang, P.J. Chang, P. Angelos, E.L. Kaplan, R.H. Grogan
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): A. Uppal, P. Angelos, R.H. Grogan
Study supervision: A. Uppal, P. Angelos, R.H. Grogan

Grant Support

R.H. Grogan was supported by award number K12CA139160 from the NCI.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked advertisement in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Received March 20, 2015; revised June 4, 2015; accepted June 8, 2015; published OnlineFirst July 9, 2015.
References

18. Malone MK, Zagzag J, Ogilvie JB, Patel KN, Heller KS. Thyroid cancers detected by imaging are not necessarily small or early stage. Thyroid 2014;24:314–8.
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, et al.

Cancer Epidemiol Biomarkers Prev 2015;24:1327-1331. Published OnlineFirst July 9, 2015.

Updated version

Access the most recent version of this article at:
doi:10.1158/1055-9965.EPI-15-0292

Cited articles

This article cites 19 articles, 4 of which you can access for free at:
http://cebp.aacrjournals.org/content/24/9/1327.full#ref-list-1

Citing articles

This article has been cited by 3 HighWire-hosted articles. Access the articles at:
http://cebp.aacrjournals.org/content/24/9/1327.full#related-urls

E-mail alerts

Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions

To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions

To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.