Management of PET diagnosed thyroid incidentalomas in British Columbia Canada: Critical importance of the PET report

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A B S T R A C T
Background: PET diagnosed thyroid incidentalomas (TI) should undergo prompt evaluation due to a high risk of underlying malignancy. Our study reviewed physician management of PET diagnosed TIs in British Columbia (BC), Canada.

Methods: All PET reports from BC between 2011 and 2014 were reviewed. Clinical and demographic data was obtained for TI patients through chart review and mail out surveys to physicians. Statistical analysis was performed to identify factors associated with further TI investigation.

Results: 4.7% PET scans diagnosed TIs in 5.3% of patients. 9.8% of diffuse and 46.1% of focal TI cases underwent ultrasound ± biopsy. PET scan report characteristics were significantly associated with further TI investigation (p-value <0.05).

Conclusions: Patients with PET diagnosed TIs are being under-investigated in BC and PET scan report related factors were found to be significantly associated with undergoing further TI workup.

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Introduction

Positron emission tomography (PET) scanning is a functional imaging technique that is used to diagnose, stage, and validate response to treatment of cancer patients. The tracer most commonly used in PET scans is 18-fluoro-2-deoxy-D-glucose (FDG), which is a glucose analog that is taken up into cells, phosphorylated by hexokinase, and subsequently becomes trapped intracellularly. Tissues with a higher metabolic rate for glucose, such as cancer, will accumulate higher concentrations of FDG intracellularly and demonstrate higher activity on PET scans.1 Thyroid incidentalomas (TI) are thyroid lesions diagnosed in patients with imaging studies that are being conducted for an unrelated reason. When imaging the neck with a PET scan for reasons other than diagnosing or evaluating thyroid disease, incidental abnormal thyroid uptake may be observed in 2–4% of patients.2–4 The pattern of uptake by the thyroid gland may have either a focal or diffuse distribution.1 FDG is not a cancer-specific agent, and an increased uptake of FDG by the thyroid gland may be due to inflammation rather than malignancy.5–7 This is especially true for diffuse TIs, as the finding is most commonly related to hypothyroidism or autoimmune thyroiditis.3–5 Diffuse TI’s have been reported to have a 4.2% risk of malignancy,5 and focal TIs have a much higher cancer risk that is approximately 35%.5,6,8

The American Thyroid Association (ATA) has published guidelines for the management of thyroid nodules and thyroid cancer. The 2015 ATA guidelines recommend that FDG-avid nodules should undergo prompt evaluation with ultrasound (US), followed by fine needle aspiration (FNAB) if the nodule is 1 cm or larger in size.2 For diffuse TIs, the guidelines acknowledge that they most often represent benign disease, but still encourage prompt sonographic examination to ensure that there is no clinically significant nodularity.2 Similarly, the American College of Radiology (ACR) recommends that patients with PET diagnosed focal TIs should, if the patient does not have any serious comorbidities or a significantly...
limited life expectancy, undergo both an US and FNAB.\textsuperscript{11}

There currently is no standardized management protocol for TIs that are diagnosed by PET scans at the British Columbia Cancer Agency (BCCA) in British Columbia (BC) Canada. The primary study objective is to retrospectively characterize the practice patterns of BC physicians upon discovery of a PET diagnosed TI, and identify factors associated with further TI workup. The secondary study objectives include determining if there is a maximum standardized uptake (SUVmax) threshold that would assist in diagnosing focal TIs as being malignant, and if the SUVmax value of malignant focal TIs are associated with any papillary thyroid carcinoma (PTC) clinical or pathological disease prognosticators. As essentially all PET scans in BC are performed at a single site, the current study is able to answer this question at the population level.

2. Material and methods

This retrospective study was carried out at the BCCA located in Vancouver, BC, Canada. The reports of all PET scans performed in BC for non-head and neck indications, between 2011 and 2014, were reviewed and patients diagnosed with TIs were identified. Exclusion criteria included: individuals who had a known primary head and neck cancer diagnosis including thyroid cancer, individuals with known widespread metastatic disease that involved the head and neck, individuals younger than 18 years of age, and individuals who underwent a PET scan using tracers other than FDG. Patient characteristics, investigations, and management were retrospectively reviewed from medical records. For patients who had no documented TI investigation, the physician who ordered the PET scan by which it was diagnosed was contacted by a letter that explained the study, outlined the clinical significance of a TI, and included a survey that requested further information on the case. Physicians of patients who were documented to be deceased within 12 months of their PET TI diagnosis were excluded from the survey.

Statistical analysis was performed using Fisher’s exact test to assess variables that may be associated with investigation of TIs. The Benjamini–Hochberg procedure was used for multiple testing correction. Patients were grouped as either having diffuse or focal TIs for each analysis where relevant. A receiver operating characteristic (ROC) curve was used to select a possible SUVmax threshold at which focal TIs were more likely to be malignant. Separately, the SUVmax of malignant focal TIs was also evaluated for its association using Fisher’s exact test with the following PTC clinical and pathological prognosticators: patient age, PTC subtype, extrathyroidal extension, nodal metastases, cancer multifocality, PTC size, and patient MACIS score.

3. Results

A total of 19,270 PET scans were performed on 15,229 patients between 2011 and 2014 for non-head and neck indications. 899 PET scans (4.7%) diagnosed TIs in 802 patients (5.3%). 342 PET scans (1.8%) diagnosed diffuse TIs and 557 PET scans (2.9%) diagnosed focal TIs. Of the 802 patients, 308 (20.4%) had diffuse TIs and 494 (32.2%) had focal TIs. Study patient and PET scan report characteristics are summarized in Table 1.

We sent mail-out surveys to 195 physicians regarding the 442 patients who had no documentation of further TI investigation. A repeat mail-out survey was sent to the physicians of the 265 patients whose initial survey was not returned after 3 months. In total, 195 surveys were returned (44.1%), 10 of which were returned blank. 95 of the 185 (48.7%) physicians who returned completed surveys stated they were aware of their patient’s TI diagnosis. Overall, there was adequate data from chart review and mail out surveys for 726 study patients. A flow diagram summarizing patient investigations and management is presented in Fig. 1.

Of the 286 patients diagnosed with diffuse TIs, 73 (25.5%) underwent one or more of the following: thyroid stimulating hormone (TSH) measurement, US, FNAB, specialist referral, or instructed to follow up with the patient’s GP. 26 (9.1%) were referred to a specialist or were instructed to follow up with their general practitioner (GP) for further TI management. 28 (9.8%) underwent at least an US ± FNAB. Of the cases that underwent an US ± FNAB, 10.7% (n = 3) were found to have malignant cytology (1 medullary thyroid carcinoma, 1 PTC, and 1 lymphoma). The diffuse TI finding was included in the final impression in 32.4% (n = 134) of PET reports describing diffuse TIs.

Of the 440 patients with focal TIs, 231 (52.5%) underwent one or more of the following: TSH measurement, US, FNAB, specialist referral, or GP follow up. 91 (20.7%) were referred to a specialist or were instructed to follow up with their GP for further TI management. 203 (46.1%) patients underwent at least an US ± FNAB. Of the cases investigated with US ± FNAB, 43 (21.2%) were found to have malignant cytology, and 36 (17.7%) were confirmed to be thyroid cancer by surgical pathology (34 PTC and 2 follicular carcinomas). The average size of PTC was 1.2 cm (range 0.2–3.2 cm), and papillary microcarcinoma (PTC<1 cm) accounted for 44.1% (15/34) of these cases. The 7 other cases with malignant cytology were not operated on. The focal TI finding was included in the final impression in 85.7% (n = 377) of PET reports describing focal TIs.

### Table 1

<table>
<thead>
<tr>
<th>Variable Evaluated</th>
<th>Value</th>
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<tbody>
<tr>
<td>Total number of TI patients</td>
<td>802</td>
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<tr>
<td>Age in years at time of scan, median (range)</td>
<td>67 (22–92)</td>
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<tr>
<td>Gender, n (%)</td>
<td>Female 589 (73.4), Male 213 (26.6)</td>
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<tr>
<td>Year of PET Scan, n (%)</td>
<td>2011 107 (13.3), 2012 208 (25.9), 2013 185 (23.1), 2014 302 (37.7)</td>
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<td>Primary Malignancy Type, n (%)</td>
<td>Breast 104 (13.0), Gastrointestinal (GI) 191 (23.8), Gynecological (Gyne) 70 (8.7), Lung 302 (37.7), Lymphoma 71 (9.0), Other: 22 (2.7)</td>
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<td>Finding, n (%)</td>
<td>Not reported 246 (79.9), Diffuse 308 (38.4), Focal 494 (61.6)</td>
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<td>SUVmax of diffuse TIs, n (%)</td>
<td>Not reported 9 (2.9), &lt;3.3 30 (9.7), 3.3—6.5 9 (2.9), 6.6—9.8 12 (3.9), &gt;9.9 11 (2.6)</td>
</tr>
<tr>
<td>SUVmax of focal TIs, n (%)</td>
<td>Not reported 65 (13.2), &lt;3.3 203 (41.1), 3.3—6.5 72 (14.6), 6.6—9.8 12 (3.9), &gt;9.9 53 (10.7)</td>
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<tr>
<td>Inclusion of the TI finding in PET report final impression, n (%)</td>
<td>Diffuse TIs 146 (47.4), Focal TIs 429 (80.8)</td>
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</table>
| Further TI evaluation suggested in PET report, n (%) | Diffuse TIs 109 (22.1), Focal TIs 430 (87.0)
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