ABSTRACT

Background: Thyroid incidentalomas detected by 18F-Fluorodeoxyglucose Positron Emission Tomography (FDG-PET) have been reported in 1.1 to 2.9% of scans performed. Previous studies have determined the prevalence of thyroid malignancy in these patients to be 14-72%.

Objective: We undertook a retrospective study to determine the prevalence of thyroid incidentalomas in our center, and evaluated the corresponding prevalence for malignancy in these patients.

Results: A total of 2,912 FDG-PET scans were performed on 1,855 patients, of which 56 (3.0%) presented with a thyroid incidentaloma (40 focal and 16 diffuse). Among the 22 patients who had an ultrasound, 15 presented with solid nodules (10 focal and 5 diffuse), while 5 were negative for any lesions (4 focal and 1 diffuse). Of 13 patients who had a subsequent FDG-PET scan, 8 had resolution of the hypermetabolic foci (61.5%), of which 5 were focal and 3 diffuse. Only 1 of 6 incidentalomas whose histological diagnoses were available showed malignancy (papillary carcinoma). Other cytologic diagnoses include colloid goiter and lymphocytic thyroiditis.

Conclusion: The prevalence of thyroid malignancy in focal incidentalomas is 1 in 12 (8.3%) and 1 in 17 in all incidentalomas (5.9%). Our experience indicates that the prevalence rates are much lower than that previously reported. Nevertheless, the prevalence rates are significantly elevated to warrant further evaluation, including an imaging procedure and fine needle aspiration biopsy.

Keywords: Thyroid incidentaloma, thyroid carcinoma, positron emission tomography

INTRODUCTION

Positron emission tomography (PET) is a non-invasive method for screening and evaluating the whole body for various kinds of malignancies. It requires the use of molecules that are labeled with radioactive nuclides, among which 18F-Fluorodeoxyglucose is most commonly used. Because cancer cells exhibit increased rate of glycolysis, 18F-Fluorodeoxyglucose positron emission tomography (FDG-PET) is able to assess a fundamental alteration in the cellular metabolism of glucose that is common to all neoplasms. Increased cellular glucose uptake, and likewise 18F-Fluorodeoxyglucose, is one of the key alterations associated with the high glycolytic rate of cancer cells.

Incidentalomas have been reported on FDG-PET. A thyroid incidentaloma is defined as a newly identified thyroid lesion encountered during an imaging study. One small series suggests a high rate of cancers in these incidentalomas, in which 5 of 7 patients (71.43%) presented with a malignant histology. Larger studies have reported prevalence rates ranging from 14% to 50%. These studies are summarized in Table I.

Corresponding standard uptake values (SUV) of incidentalomas are available, although its use in differentiating benign from malignant lesions has not been established. Kim et al. reported that there was no significant difference in maximum SUV between benign and malignant nodules, while Kang et al. concluded that incidentalomas with high standard uptake values (SUV) carry a higher risk of malignancy. De Geus-Oei et al. recommended that SUVs not be relied on in the discrimination between malignant and benign thyroid lesions.

Since its inception in 2001, the FDG-PET scan of the St. Luke’s Medical Center in Manila has been used in a large number of patients in the region. Many thyroid incidentalomas have been discovered during the seven-year period, although few have undergone further evaluation. The objectives of the study are to identify the prevalence of thyroid incidentalomas identified by FDG-PET and the prevalence of malignancy in these patients.
MATERIALS AND METHODS

Subjects

The data and images from all FDG-PET studies conducted from 10 January 2002 to 31 December 2007 were analyzed retrospectively. FDG-PET is performed at our institution for several indications: as a cancer-screening program in presumptively healthy subjects; as the initial evaluation for a tumor visualized by another imaging procedure; as a method for establishing tumor extent or staging; as a means for assessing a patient's response to cancer treatment; and as a tool for determining tumor recurrence in patients treated for malignancies.

All scans during the study period in which a thyroid incidentaloma was reported were retrieved for inclusion in the study. Other data from the subjects included in the study were collected from the institution’s central computer and physicians records, including results from laboratory procedures and other imaging studies. Subjects were grouped according to the appearance of the incidentaloma (focal vs. diffuse). Patients with pre-existing thyroid carcinoma were excluded.

FDG-PET Method

FDG-PET scans were obtained on a whole body PET scanner (GE Advance Nxi PET Scanner). All patients fasted for at least 6 hours prior to the study. Image acquisition for the whole body scan was performed from the head to the mid-thigh 60 minutes after administration of 10 to 20mCi $^{18}$F-FDG. 5-minute positron emission and 3 minute transmission images were acquired. Transmission, attenuation and non-attenuation corrected images were processed and read. Maximum weight normalized SUVs were calculated around each lesion. All FDG-PET scans were interpreted by one reader (JS).

RESULTS

We reviewed 2,912 FDG-PET scans performed on 1,855 patients, and identified 56 (3%) with thyroid incidentalomas. The characteristics of selected patients with focal and diffuse thyroid incidentalomas are presented in Tables II and III, respectively. The evaluation of breast, lung and colon cancers were the most common indications for requesting a FDG-PET scan in these patients. The age distribution is presented in Figure 1.
Of the incidentalomas, 40 (2.2%) were of the focal type and 16 (0.9%) were of the diffuse type. Among the patients with focal thyroid incidentalomas, 30 were female and 10 were male, with an average age of 56.8 years (range 21-89 years). Sixteen of the thyroid incidentalomas were located in the right lobe, 20 in the left lobe, and 4 in both lobes. The average standard uptake value (SUV) for all foci was 8.0 (range 2.9-19.8). Of the 15 patients whose thyroid ultrasound or CT scan was available, only 10 (66.67%) had a corresponding thyroid nodule. One (6.67%) patient had a complicated cyst, while the remaining 4 (26.67%) did not have any thyroid lesions.

In the patients with the diffuse thyroid incidentalomas, 11 were female and 5 were male. The average age was 57 years (range 36-69 years). Seven patients had a subsequent thyroid ultrasound done, among which five (71.4%) presented with a thyroid nodule or mass, one (14.3%) with a thyroid cyst and one (14.3%) with an unremarkable thyroid. Figure 2 shows an image of a patient with a diffuse thyroid incidentaloma.

Among the 13 patients who had a subsequent FDG-PET scan, 8 (61.5%) had resolution of the hypermetabolic foci (5 of which were of the focal type, and 3 of the diffuse type). Six patients underwent fine needle aspiration biopsy (4 from the focal group and 2 from the diffuse group). Fine needle aspirations were performed by different physicians, but examined by one cytologist. Both patients from the diffuse group had benign cytology (colloid goiter and lymphocytic thyroiditis). Three patients from the focal group were found to have colloid goiter on cytology, while one patient, a 34 year-old female with no prior malignancy and a maximum SUV of 5.9, presented with papillary cancer (Figure 3). The malignancy was later confirmed by surgical histology.

DISCUSSION

Thyroid nodules are common disorders in Endocrinology. Prevalence studies estimate the rate of palpable thyroid nodules to be 3-7% in North America. The prevalence of thyroid nodules on ultrasound has been estimated to be 20-76%. Despite the high frequency, malignant lesions account for only 5% of all thyroid nodules, independent of size.

The prevalence rate of thyroid incidentalomas on FDG-PET ranges from 1.1-2.9% in an unselected population, and 1.6% in healthy subjects. There has been no report about the prevalence of FDG-
PET-positive-thyroid incidentalomas in the general population. Given the high cost of a FDG-PET procedure and the low prevalence of an incidentaloma, it is unlikely that its use as a screening procedure for thyroid malignancies will be of significant benefit in the general population.

Previous studies on thyroid incidentalomas have centered only on focal hypermetabolic lesions rather than the diffuse type. In our study, 71.4% of the patients from the diffuse group who underwent a thyroid ultrasound had a solid nodule or mass, compared to only 66.67% from the focal group. Although only two of these patients had a subsequent thyroid biopsy, of which both were benign, we believe that further work-up of these incidentalomas remains warranted.

A number of patients with incidentalomas in our study presented with negative findings on ultrasound or CT scan as part of further evaluation (26.7% in the focal group, and 14.3% in the diffuse group). Such occurrence has also been reported by Yi et al., in which 2 of 6 patients with FDG-PET thyroid incidentalomas were negative for nodules on CT or sonogram. These lesions were therefore considered benign, and biopsy not indicated. The management guidelines for patients with thyroid nodules, as developed by the American Thyroid Association, recommends no further work-up for ultrasound-negative thyroid glands. It may be acceptably safe to assume that despite hypermetabolic activity on FDG-PET, the absence of a lesion on ultrasound or CT is adequate evidence to rule out a malignant lesion.

Among subjects who had a subsequent FDG-PET scan, 61.5% had resolution of a reported hypermetabolic focus. Such occurrences have not been reported in the literature. Given the very high negative predictive value for detecting malignancy in the preoperative evaluation of thyroid nodules, the assumption that such foci are truly benign should be considered. The question of why a foci was initially noted prompts us to review the principles of FDG-PET. FDG-PET preferably picks up malignant lesions because of the increased rates of glycolysis and glucose uptake. One of the glucose transport proteins, GLUT 1, has been found to be expressed at high levels in a variety of cancers. By immunostaining, GLUT 1 expression was frequently detectable in differentiated and anaplastic thyroid carcinoma, but not in benign nodules or normal thyroid. FDG is not cancer specific, and will accumulate in sites with high levels of metabolism and glycolysis, such as in hyperactivity, active inflammation and tissue repair, which may explain the transient hypermetabolic foci seen in some patients.

With the addition of several patients who may be assumed to have a non-malignant thyroid, either due to the absence of a lesion on ultrasound or CT scan or due to resolution of the focus on a subsequent FDG-PET scan, the prevalence of thyroid malignancy in focal incidentalomas is 1 in 12 (8.3%) and 1 in 17 in all incidentalomas (5.9%). Our experience indicates that the prevalence rates are much lower than that previously reported.

Despite these relatively lower results, the prevalence rates are significantly elevated to warrant further evaluation, including an imaging procedure, such as ultrasound, and corresponding fine needle aspiration biopsy.

Limitations of the study include the limited availability and potential inaccuracy of medical records used in a retrospective study. There is also a lack of priority in performing further diagnostic tests on thyroid incidentalomas, mainly because FDG-PET scans are requested for the evaluation of another malignancy, and priority is focused on the primary cancer. A more appropriate setting for such a study would be a prospective study.

**CONCLUSION**

Of the 1,855 patients who underwent FDG-PET scanning showed thyroid incidentaloma (40 focal and 16 diffuse). Patients who had an ultrasound from both groups presented with solid nodules (66.67% focal and 71.4% diffuse), indicating that further work-up may be warranted in both groups. Despite the lack of a definitive cytological or histopathological diagnosis in many patients, the assumption that malignancy can be ruled out in certain subjects indicates that the prevalence of thyroid malignancy in focal incidentalomas is 1 in 12 (8.3%) and 1 in 17 in all incidentalomas (5.9%). Our experience suggests that the prevalence rates are much lower than that previously reported.

**REFERENCES**


