

# Evaluation of Incidental Thyroid Nodules in Cancer Patients

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**Abstract:** Objective: Frequency of thyroid cancer in incidental thyroid nodules identified by imaging techniques in cancer patients is higher than that in the normal population. In the retrospective study, we have both investigated the incidence of thyroid cancer in incidentally identified nodules and compared the imaging techniques to determine whether there is any difference between them in detection of malign nodules.

**Methods:** A total of 7319 patients who underwent thyroid fine-needle aspiration biopsy (FNAB) were included in the study. The data of 174 patients who had previously been diagnosed with a hematologic or solid malignancy prior to the FNAB procedure and had incidentally identified thyroid nodules were evaluated retrospectively.

**Results:** Eighty-six (49.5%) of the incidental nodules were identified with ultrasonography (USG), 62 (35.6%) with positron emission tomography (PET) or PET/computed tomography (PET/CT), and 26 (14.9%) with CT. As a result of thyroidectomy, papillary carcinoma was identified in 8 (4.6%) patients, and metastasis to the thyroid of a primary cancer was found in 3 (1.7%) patients. While the papillary carcinoma proportion in the nodules identified by USG was 3.4%, PET/CT was 8.9%. A cut-off maximal standardized uptake value of 11.6 in PET/CT indicated malignancy achieving a sensitivity of 83.3% and a specificity of 91.1%.

**Conclusion:** Whether the nodule in the incidental thyroid nodules of cancer patients is identified using USG or PET/CT, the risk of thyroid cancer is similar. However, cancer risk is higher in the event of a higher focal uptake in the nodules identified by PET/CT.

**Keywords:** Incidental thyroid nodule ■ Thyroid cancer ■ Second malignancy

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## INTRODUCTION

While incidental thyroid nodules are detected by ultrasonography (USG), computed tomography (CT) and magnetic resonance imaging (MRI) during an overall medical check-up or evaluation of benign diseases such as parathyroid diseases, pulmonary

diseases and traumatic injuries, they are detected by positron emission tomography (PET) or PET/computed tomography (PET/CT) usually during cancer screening or in people with a known malignancy. Frequent use of imaging modalities and their increased sensitivity significantly increased the identification of incidental thyroid nodules.<sup>1,2</sup> They are predominantly identified by USG (67%),<sup>3</sup> followed by a 16% identified by MRI,<sup>4</sup> whereas 9.4% is identified by carotid duplex scan<sup>5</sup> and 2-3% is identified by PET or PET/CT scan.<sup>6</sup>

Although the malignancy rate of the incidental thyroid nodules in a healthy population is quite low, the cancer rate in incidental thyroid nodules, especially in those identified by PET/CT in patients with non-thyroidal malignancies, is significantly high (8.6-29%).<sup>7-12</sup> In addition, Ronckers et al, using Surveillance, Epidemiology and End Results (SEER) cancer registry, have shown that the patients with non-thyroidal malignancies have a 42% higher risk of developing thyroid cancer than the normal population. Moreover, they have identified that this increased risk is most frequently ensues in breast, prostate, colon cancers and melanoma.<sup>13</sup>

In patients with a non-thyroidal malignancy, the studies that investigate incidental thyroid nodules and any thyroid cancer in them are usually PET or PET/CT studies. There are not many studies that investigate the frequency of thyroid cancer in the nodules identified in cancer patients by other imaging techniques. Therefore, in this study, we investigated the frequency of thyroid cancer in patients with known non-thyroidal malignancies who have incidental thyroid nodules identified by any of the USG, CT or PET or PET/CT imaging modalities. Moreover, we aimed to identify which type of primary cancer patients followed up by our center have an increased thyroid cancer incidence rate.

## MATERIAL AND METHODS

### Patients

During a course of 7 years, 7319 patients that underwent thyroid fine-needle aspiration biopsy (FNAB) in the department of endocrinology at a university hospital due to thyroid nodule were included in the study. Medical records of the patients were used to identify whether or not they

were diagnosed with a solid or hematologic malignancy any time before the thyroid biopsy. A total of 7145 patients who were not diagnosed with any malignancy prior to the biopsy or were ineligible to the study as per exclusion criteria were excluded and the data of the remaining 174 patients were retrospectively evaluated.

A detailed record about the reason of underwent imaging modality (USG, CT, PET/CT) (cancer staging, evaluation of jugular venous pathologies, evaluation of parathyroid lesions or LAP studies) was kept. Patients were classified and analyzed by the imaging modality their thyroid nodules were identified. Exclusion criteria were as follows:

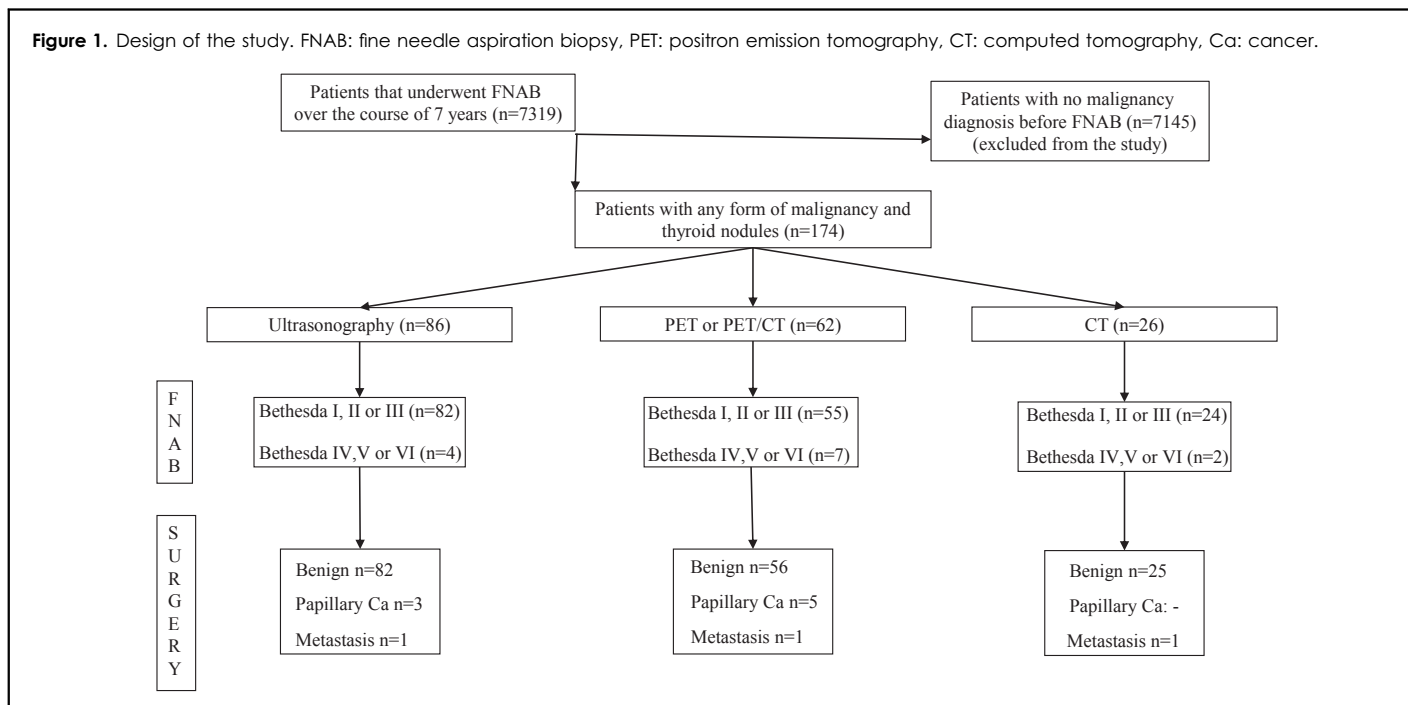
- 1 - Younger than 18 years of age
- 2 - No record of solid or hematologic malignancy diagnosis before FNAB
- 3 - A positive history of thyroid disease or previous medical treatment for a thyroid disease
- 4 - Imaging modality performed because of thyroid disease

Demographic information, time of diagnosis and stage of the primary malignancy, whether or not the patient got radiotherapy, and whether or not the primary cancer is in remission were identified from the patients' medical records and saved. Whether or not the patients got active chemotherapy was not taken into account. Staging of the primary cancer and thyroid papillary cancer were done according to Tumor Node Metastasis (TNM) System

recommended by American Joint Committee on Cancer (AJCC). Design of the study is depicted in [Figure 1](#).

### Evaluation of the thyroid nodule

Whether or not there was a focal or diffuse uptake and maximal standardized uptake value (SUVmax) were recorded for patients with thyroid nodules identified by PET/CT. Before FNAB, thyroid USG was performed on each patient and nodule size, shape, vascularity characteristics, echogenicity and presence of microcalcification, if any, were re-evaluated and the following findings were recorded in terms of malignancy criteria: a – hypo-echogenicity, b – punctate microcalcifications, c – irregular margins, d – a shape that is taller than its width, e – increased intranodular vascularity, f – an incomplete peripheral halo.<sup>14</sup> Based on the hormonal evaluation of the patients, those with thyrotoxicosis got a thyroid scintigraphy and according to the results, patients with a hyperactive nodule were excluded. FNABs of all patients included in the study were carried out under USG-guided by an experienced endocrinologist. In patients with more than one nodule, biopsy was performed on all nodules greater than 1 cm. In case of subcentimetric nodules on the other hand, biopsy was performed only on those with at least one ultrasonographically-identified malignancy criterion or in the event of focal uptake identified in PET/CT. FNAB results of the patients were classified according to the Bethesda criteria.<sup>15</sup> Category I—nondiagnostic or unsatisfactory, Category II—benign, Category III—atypia of undetermined significance or follicular lesion of



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