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Effectiveness of Hounsfield Unit Values in the Differentiation of Malign and Benign Thyroid Nodules

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ABSTRACT

Thyroid nodules are today encountered more frequently due to the advances in imaging methods. Here, we aimed to evaluate the efficacy of computed tomography Hounsfield Unit (HU) values in the differential diagnosis of benign or malign thyroid nodules. This retrospective study involved 51 patients with thyroid nodules who had thyroid fine needle aspiration biopsy (FNAB) result and chest computed tomography (CT) with or without contrast-enhanced, between January 2018 and September 2020. Circular ROIs (region of interest) were drawn on the section that best demonstrated the thyroid nodule on CT and obtained HU values were averaged. An independent t test was applied to the HU values for the malign-benign differentiation. Of the 40 patients who had contrast-enhanced CT, 25 were benign and 15 were malign. Of the 11 patients who had non-enhanced CT, 6 were benign and 5 were malign. In contrast-enhanced scans, nodule attenuation was statistically significantly higher in malign nodules (116.26±17.74 HU) when compared with benign nodules (93.84±24.33 HU) (p= 0.004). A receiver operating characteristic (ROC) analysis revealed an area under the curve of 78.8%. The sensitivity and specificity of the cut-off value of 104.5 for the area under the curve were found to be 80% each. In non-enhanced scans, nodule attenuations were not significantly different in malign (49±12.14 HU) and benign (67.5±16 HU) nodules (p= 0.72). Considering the possibility of malignancy in thyroid nodules, the thyroid gland should be evaluated carefully with thoracic CT. Sonographic correlation is recommended for nodules with a HU value of 104.5 and above detected on contrast-enhanced tomography images.

Keywords: Thyroid nodule, Computed tomography, Hounsfield unit, Malignancy

Introduction

Incidental thyroid nodules are common in the adult age group. Thyroid nodules are today encountered more frequently due to the advances in such imaging methods as computed tomography (CT), ultrasonography (US) and magnetic resonance imaging (MRI). Thyroid nodules are identified incidentally in 20–68%, 25% and 16–18% of patients by ultrasonography, contrast-enhanced CT and MRI, respectively (1,2,3). Female/male ratio is 4/1 for thyroid nodules. Nodule prevalence increases with age and almost 50% of women above the age of 70 years are found to have a thyroid nodule (4). The increase in the rate of diagnosis of nodules, in addition to the advances in radiological imaging, has led to more thyroid fine needle aspiration biopsies (TFNAB) being performed, and thus an increase in the incidence of thyroid cancer (1,5).

No reliable criterion has yet been identified for the diagnosis and reporting of the potential of malignancy of thyroid nodules by CT or MRI, in contrast to US (6), and so reports of radiologists of the suitability of CT and MRI for the identification of thyroid nodules are rather variable. Among them, some radiologists report all nodules due to the malignancy potential of thyroid nodules, while others may not report them all, since thyroid cancers are rare in incidental nodules, and small thyroid cancers have a silent clinical picture in general (7, 8, 9).

The frequency of determination of incidental nodules in thyroid gland has increased with the advances in CT imaging in current practice. Here, we evaluate the efficacy of Hounsfield Unit (HU) values in the differentiation of the diagnosed thyroid nodules as benign or malign.

Materials and Methods

Patients: The ethical approval of this retrospective study is available (2020/03-13), and a signed informed consent form was received from all participants. The records of a total of 563 patients in the radiology archive who underwent thyroid FNAB in the interventional radiology unit between January 2018 and September 2020 were screened retrospectively. Among these cases; 66

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Table 1. Hounsfield unit values measured on CT of benign and malign thyroid nodules

	Benign nodules	Malign nodules	
Enhanced-CT	N:25 Mean HU±SD: 93,84±24,33	N:15 Mean HU±SD: 116,26±17,74	p=0.004
Non-enhanced-CT	N:6 Mean HU±SD: 67,5±16,89	N:5 Mean HU±SD: 49±12,14	p=0.72

patients with contrast enhanced or non-enhanced chest CT with thyroid nodules of at least 1 cm in size were evaluated. Nodules with an image that included artefacts (3 patients), patients in whom the whole thyroid gland was not included in the CT sections (2 patients), those with nondiagnostic pathology result (1 patients), those with more than one nodule in a single lobe (4 patients), those with pure cystic nodules or nodules with a small solid component that was inadequate for measurement or pure calcified nodules (3 patients), and those with nodules that were not clearly identified by CT (2 patients) were excluded from the study. This study was concluded with 51 patients (40 contrast enhanced, 11 non-enhanced CT scan) who matched the inclusion criteria.

Imaging: Computed tomography images were obtained using a multislice CT [Somatom Emotion 16-slice; CT2012E- Siemens, Germany, 16 slice, 120 kV, 200 effective mA, 3 mm slice thickness, 0.6 sec (rotation time)] device. For routine contrast enhanced chest CT imaging, 80 ml of non-ionized contrast material, iohexol (Amersham Health, Ireland) or iopromide (Schering, Germany) was injected into the forearm vein at a rate of 3 mL/sec. using an automated injector (CT 9000 ADV Liebel-Flarsheım). Sections from the lower slices of the neck to the upper abdomen were obtained during CT imaging with or without contrast enhancement, with the patients in a supine position. A radiologist with 6 years of experience using a medical monitor with high resolution and gray tone for the CT evaluations, regardless of the pathology results, took 3 mm thickness axial and multiplanar reformat images that had been previously obtained and transferred to the system, and evaluated them for CT-HU measurements. Computed tomography images, ultrasound reports and the thyroid FNAB reports were correlated to verify that the CT-HU measurement was performed from the nodule that was performed on FNAB. Circular ROIs (region of interest) with an area of 0.5-0.55 cm^2, varying from 1 to 3 depending on the size of the nodule, were drawn on the section that best demonstrated the thyroid nodule in axial images and obtained HU values were averaged. Attention was paid not to include the neighboring thyroid parenchyma and the calcifications in the measurement area. Subsequently, benign and malign classification were made separately from contrast-enhanced and non-enhanced CT, taking into account the TFNAB results of each patient.

Statistical Analysis: An independent 2-sample t test was used to statistically compare the malign and benign thyroid nodule with HU values, and the receiver operating characteristic (ROC) curve was used to evaluate the cut off values. The necessary statistical analyse was performed using SPSS statistical software. The statistical significance level was set at 5% in the calculations. The sensitivity and specificity percentages were obtained.

Findings: Fifty-one patients with a minimum size of 10 mm and a maximum size of 64 mm in the long axis of the nodule were included. The mean age of the patients who had malign and benign nodule were 58.15±13,95 (range: 26-90 years) and 53.68±13.42 (range: 27-89 years) respectively. Based on the cytology results, 20 (39.2%) patients were classified as malign and 31 (60.8%) as benign. Of the 20 patients with malign nodule, 14 (70%) were female and 6 (30%) were male. Of the 31 patients with benign nodule, 23 (74.19 %) were female and 8 (25.81%) were male. An intravenous contrast material was used in 40 patients, while no contrast material was used in 11 patients. Among the 40 patients who had contrast-enhanced CT, 15 cases had malign and 25 cases had benign nodules. Among the 11 patients who had non-enhanced CT, 6 cases had benign and 5 cases had malign nodules (Table 1).

The mean attenuation values of 40 patients who were administered intravenous contrast material were calculated as 116.26 ± 17.74 (79-141) HU for patients with malign nodules and 93.84 ± 24.33 (42-146) HU for patients with benign nodules (Figures 1 and 2). A statistically significant

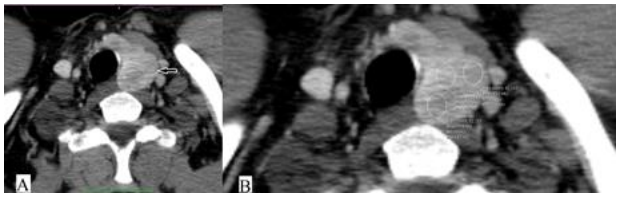

Fig. 1. A 56 year-old male with a malign thyroid nodule. A: Contrast-enhanced CT scan demonstrates 29-mm well-circumscribed nodule in the left thyroid lobe (arrow). B: Three separate ROIs with an area of 0.5-0.55 cm² were drawn and the mean attenuation of the nodule calculated as 130 HU

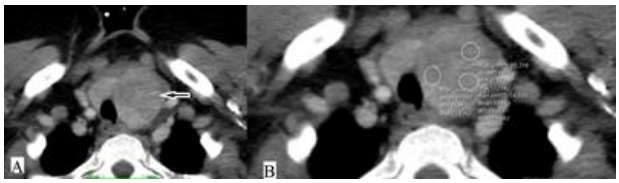

Fig. 2. A 51 year-old female with a benign thyroid nodule. A: Contrast-enhanced CT scan demonstrates 45-mm well-circumscribed, heterogenous, hypodense nodule in the thyroid left lobe (arrow). B: Mean attenuation of the nodule calculated as 81.3 HU

difference was identified in an independent t test performed to differentiate the malign and benign thyroid nodules in the patients administered an intravenous contrast material (p= 0.004). A ROC analysis, performed to obtain the cut-off value, revealed an area under the curve of 78.8%. The sensitivity and specificity of the cut-off value of 104.5 for the area under the curve were found to be 80% each (Figure 3).

Among the 11 patients who were administered no intravenous contrast material, the mean attenuation value for the patients who had malign nodules was calculated as 49±12.14 (31–60) HU, and the mean HU value for the patients who had benign nodules was calculated as 67.5±16.89 (40–86) (Figures 4 and 5). There was no statistically significant difference in the independent t test that was performed to differentiate benign and malign thyroid nodules in the patients administered no intravenous contrast material (p= 0.72).

Discussion

Thyroid nodules are lesions that are frequently detected with advances in imaging technologies. The incidence of thyroid nodules vary depending on the method used to detect thyroid nodules, such as autopsy, US, CT and MRI, being between 2 and 67% (10, 11, 12). The frequency of detection of thyroid nodules in thoracic CT imaging has also increased in daily practice with the introduction of multislice CT, through which high-resolution thin sections are obtained.

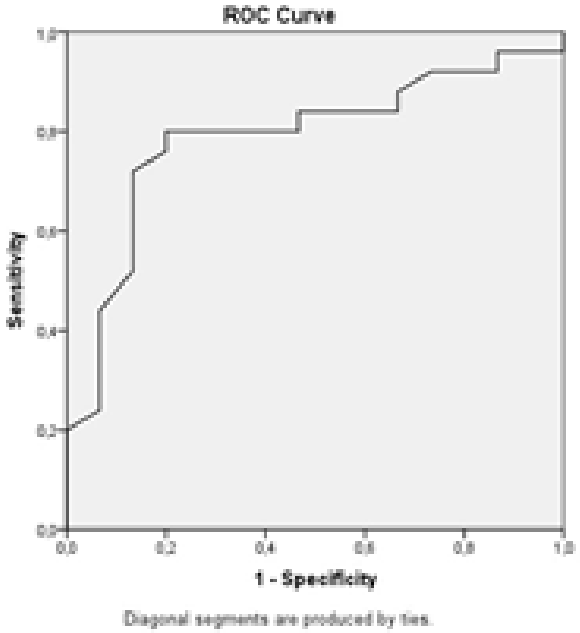

Fig. 3. Receiver operating characteristic (ROC) curves of contrast-enhanced CT when a mean attenuation value of 104,5 HU was used to differentiate malign and benign nodules

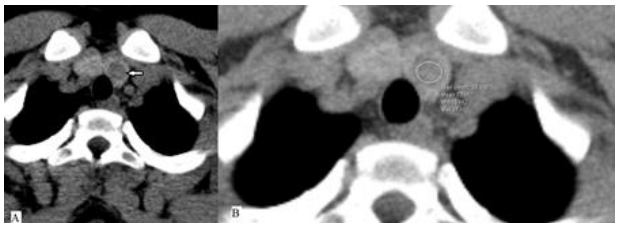

Fig. 4. A 26 year-old female with a malign thyroid nodule. A: Non-enhanced CT scan demonstrates 15-mm well-circumscribed, hypodense nodule in the thyroid left lobe (arrow). B: One ROI with an area of 0.5-0.55 cm² was drawn and the mean attenuation of the nodule was as 53 HU

Computed tomography images can be obtained with or without contrast enhancement, as thyroid nodules can easily be detected even without contrast enhancement, since normal thyroid tissue has a high intrinsic attenuation in CT (13). Incidental thyroid nodules may be encountered in up to 25% of patients undergoing contrast-enhanced CT screening (14). No reliable criteria are present to differentiate benign and malign nodules by CT, although there are certain criteria for such a differentiation for US, which is the ideal imaging method for thyroid nodules. In the present study, in which the efficacy of the HU values for the benign and malign differentiation of thyroid nodules that are diagnosed frequently by chest CT in daily practice was investigated, CT without contrast enhancement revealed no significant difference; in contrast, a statistically

Fig. 5. A 31 year-old female with a benign thyroid nodule. A: Non-enhanced CT scan demonstrates 17-mm well-circumscribed, hypodense nodule in the thyroid right lobe (arrow). B: One ROI with an area of 0.5-0.55 cm^2 was drawn and the mean attenuation of the nodule was as 63 HU

significant difference was found in contrast-enhanced CT.

Various studies have been conducted to date investigating the prevalence of thyroid nodules detected by CT. Incidental thyroid nodules were found in 55 out of 1,941 (2.8%) patients in a study by Lee et al. in their retrospective evaluation of low dose no contrast-enhanced thoracic CT images for lung cancer (15). The authors found a total of 39 benign nodules in 26 patients and 11 malign nodules in seven patients among those matching the inclusion criteria of the study. No statistically significant differences were noted in gender, age, localization, longitudinal diameter, ratio of anteroposterior/transverse diameters, margins, density, presence or pattern of calcification, and thyroid enlargement between the benign and malign nodules, while they found a mean attenuation value of 55 HU and above to be statistically significant. In this present study, no statistically significant difference was found in the attenuation values between the six benign and five malign patients in whom we obtained CT scans with no contrast enhancement, which we suggest may be due to the low number of patients in our series.

Yoon et al. reported statistically significantly high mean attenuation values in malign thyroid nodules when compared to benign nodules in a contrast-enhanced neck CT in a study in which they investigated many parameters in 105 benign and 15 malign patients (16). In the present study, in which 25 benign and 15 malign nodules were identified, the mean attenuation values measured by contrast-enhanced thoracic CT were found to be statistically significantly higher in malign nodules than in benign nodules, similar to the above-mentioned study. In addition, the nodules were classified as cystic, mixed and solid in the study by Yoon et al., and the mean HU values of the solid nodules were found to be significantly higher than those of the mixed and cystic lesions. In the present study, we measured only the solid parts of the nodules, and excluded pure cystic nodules or nodules with a small solid component that was inadequate for measurement.

The mean attenuation value was measured as 65±105 and 107±54 in CT's with no contrast enhancement (2 malign and 30 benign lesions) and in contrast-enhanced (7 malign and 70 benign lesions) CTs, respectively, in the retrospective study by Lee et al., performed between 2004 and 2011 evaluating thyroid nodules detected by neck or thoracic CT with or without contrast enhancement. No statistically significant association was found between the mean attenuation value of the nodules and the benign or malign FNAB/surgical diagnosis. In the present study, no significant difference was noted in the attenuation values in the differentiation of benign and malign thyroid nodules diagnosed in thoracic CT with no contrast enhancement. In contrast to that study, we recorded a statistical significance in thoracic CT with contrast enhancement. We concluded that the difference in the time of contrast administration during the contrast-enhanced thoracic and neck CT scans may have affected the results in the study mentioned above (17). In the present study, only nodules detected by thoracic CT were evaluated, while thyroid nodules found on neck CT were excluded, since the contrast phase was different.

The attenuation of nodules in non-contrast-enhanced CT was found to be significantly lower for malign nodules than for benign nodules in a study by Fitzgerald et al. (18) aimed at characterizing thyroid nodules through CT in 20 patients (36 and 61 HU respectively, $p = 0.05$). The authors found no statistically significant difference in nodule attenuation, between malign and benign nodules in arterial phase and delayed phase contrast images (128 and 144 HU, $p= 0.7$; 74 and 98 HU, $p= 0.3$ respectively). No significant difference was found in the mean attenuation values of benign and malign nodules in the present study, although the mean attenuation value was higher in benign nodules ($p= 0.72$). We suggest that the lower number of patients might have been an important factor.

The retrospective nature and low number of patients can be regarded as limitations of the present study. Another limitation may be the fact that the computed tomography images were not taken based on a specific protocol for contrast phase because of the retrospective nature of the study. A further limitation is that the attenuation measurements of the small thyroid nodules in the

computed tomography images may have been affected by the partial volume effect, and beam hardening artefacts due to the high attenuation of the normal thyroid parenchyma or the bones. We excluded images containing artefacts and small nodules to overcome this problem.

Conclusion

Taking into consideration the possibility of malignancy in thyroid nodules, the thyroid gland should be evaluated carefully through thoracic CT, as is the case with all other organs. In the present study, in which the efficacy of the Hounsfield Unit values for the benign and malign differentiation of thyroid nodules was investigated, CT without contrast enhancement revealed no significant difference; in contrast, a statistically significant difference was found in contrast-enhanced CT. A sonographic correlation is recommended for nodules with an HU value of 104.5 and above detected on contrast-enhanced tomography images.

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