Usefulness of Doppler ultrasound-obtained resistance index in thyroid nodules with ultrasonographic malignant characteristics

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Abstract

Introduction: Thyroid nodular disease is highly prevalent in the general population. Its diagnosis has increased with Doppler ultrasound, by means of which features suggestive of malignancy can be detected, such as resistance and pulsatility indices elevation. Objective: To assess the correlation of a high resistance index and histopathological findings in patients with ultrasonographic suspicion of malignant thyroid nodules. Method: Prospective, cross-sectional, analytic, observational study of diagnostic tests carried out at Specialty Hospital 25, in Monterrey, Nuevo León. Patients with thyroid nodules of ultrasonographic malignant characteristics were included; the resistance index of the nodules was obtained and compared with histopathological findings. Results: Forty-eight patients with ultrasonographic diagnosis of malignant nodules were included. The correlation of elevated resistance indices with malignant thyroid nodule histopathologic diagnosis was significant (p = 0.001). Sensitivity was 73.3% and specificity 78.7%; positive predictive value was 61.1% and negative predictive value was 86.6%. Conclusion: The resistance index determination is increasingly being used, but its sensitivity and specificity are low, and it is not a reliable method, and other complementary methods are therefore still required.

KEY WORDS: Thyroid nodule. Doppler. Thyroid cancer. Ultrasonography.

Introduction

Thyroid nodular disease is a highly prevalent entity in the general population, with a higher incidence in females. Its diagnosis has exponentially increased since ultrasound started being used, as it has enabled the detection of non-palpable nodules and has increased the frequency of incidental findings in non-selected patients. Estimated prevalence in the general population ranges from 4 to 7%, with a higher rate in areas with iodine deficiency. Only in the United States, 275 000 new cases of thyroid nodules are detected every year. The Framingham study found that 4.2% of the study population had nodules at initial assessment, and that females had more nodules with regard to males (6.4% of females versus 1.6% of males); during patient follow-up, 1.3% were found to have developed nodules. Thyroid cancer is the most common malignancy of the endocrine system. The incidence of thyroid cancer ranges from 1.2 to 10 per 10,000 patients, depending on the geographic area, ethnicity and previous radiation exposure; it increases with age and reaches a plateau after 50 years of age, approximately. Non-palpable nodules’ detection has dramatically increased thanks to ultrasound, by means of which, a prevalence of thyroid nodules of between 19 and 46% has been revealed in the general population. With this diagnostic resource, in addition to detecting nodules smaller than 1.5 cm in diameter, 62% of those that are clinically solitary have been found to be actually multiple. Its use is estimated to have changed the therapeutic decision in 44% of patients. Currently, especially with duplex Doppler and power Doppler ultrasound, characteristics suggestive

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of malignancy can be identified, including: marked hypoechogenicity, intranodular vascularity, incomplete peripheral halo, irregular margins, central microcalcifications, and resistance and pulsatility indices elevation. In some studies, sensitivity and specificity rates of 77 and 79 % have been found for Doppler in comparison with fine-needle puncture aspiration (FNPA), which remains the diagnostic method of choice.

**Method**

This study was developed with information from patients of either gender who underwent ultrasound and had thyroid nodules diagnosed at Specialty Hospital 25 in Monterrey, Nuevo León. Individuals lacking ultrasound interpretation were excluded from the study and those with insufficient sample pathology report or whose report was not within the research period were eliminated from the investigation.

The cases corresponded to patients who met the described criteria between July 1 and October 3, 2014. All underwent Doppler ultrasound and resistance indices assessment. The results were tabulated according to nodule definitive histology and ultrasonographic findings. Statistical significance was calculated using the chi-square test.

Variables' descriptive analysis was carried out with the Statistical Package for Social Sciences, version 17.0 (SPSS® Inc., Chicago, IL, USA).

**Results**

Forty-eight patients were found with ultrasonographic diagnosis of malignant thyroid nodule, 42 of them (87.5 %) of the female gender. Mean age was 44.4 years, with a standard deviation of 8.4 (Table 1).

Thyroid Doppler showed that 18 patients had high resistance index, with a mean of 0.98, and 30 had a low resistance index with a mean of 0.62. By means of histopathological study, 18 patients with high resistance index were confirmed to test positive for some type of thyroid malignancy; of the 30 patients with low resistance index, 4 were malignancy-positive: 3 had papillary and one medullary cancer. As for the neoplasm histopathological lineage, 9 patients (60 %) had papillary cancer, 5 (33.3 %) follicular cancer and one (6.7 %) medullary cancer reported (Table 1).

Significant difference (p = 0.001) was found when the proportion of patients with high resistance index findings and malignant thyroid nodules histopathological diagnosis was compared. High resistance index value sensitivity for the diagnosis of malignancy in nodules with ultrasonographic evidence thereof was 73.3 % and specificity was 78.7 %, with a positive predictive value of 61.1 % and a negative predictive value of 86.6 % (Table 1).

**Discussion**

In most patients with thyroid nodules at the anterior region of the neck, thyroid origin must be considered, although other possibilities should not be ruled out. The first step, once thyroid origin is corroborated, is to carry out a thorough clinical examination that enables risk factors, signs and symptoms suggestive of malignancy and thyroid dysfunction to be detected.

As for personal medical history, in addition to a history of thyroid conditions, radiation to the head or neck (a factor that increases the incidence of non-malignant thyroid nodular disease) or accidental exposure to radiation before 18 years of age should be investigated. It is important for evolution time of the nodule, nodular growth rate, existence of cervical lymphadenopathy or other symptoms such as pain or gastrointestinal obstruction to be known. In the absence of significant goiter, data consistent with tracheal compression, such as cough and dysphonia, suggest malignant lesion. Similarly, clinical data consistent with thyroid dysfunction and recent history of respiratory tract infection or pregnancy, which indicate the possibility of thyroiditis, should be investigated.

Sudden pain in the nodule or towards the occipital region is generally due to hemorrhage in a nodule and may be accompanied by a sudden increase of its volume; however, in the presence of a rapidly growing

| Table 1. Diagnostic test results on the usefulness of Doppler ultrasound-obtained resistance index in thyroid nodules with malignant ultrasonographic characteristics |
|---------------------------------|-----------|----------|
| **Gender** | **Absolute value** | **Percentage** |
| Female | 42 | 87.5 |
| Male | 6 | 12.5 |
| **Histology** | | |
| Follicular cancer | 9 | 60.0 |
| Papillary cancer | 5 | 33.3 |
| Medullary cancer | 1 | 6.7 |
| **Sensitivity** | | 73.3 |
| **Specificity** | | 78.7 |
| **Positive predictive value** | | 61.1 |
| **Negative predictive value** | | 86.6 |
nodule, it is important for the possibility of anaplastic carcinoma or lymphoma to be considered.6

Currently, ultrasonography applied to the study of the thyroid gland is widely accepted, and serves to support the study of both diffuse and local pathology; however, in spite multiples attempts to identify ultrasonographic signs in order to arrive to an etiologic diagnosis8, it is still impossible for the benign or malignant nature of a malignant thyroid nodule to be specified solely by means of standard ultrasonography.10 The most important modality in solitary thyroid nodule diagnosis is still FNPA, owing to its high diagnostic reliability.11

Systolic and diastolic rate values in papillary carcinomas were lower than in the rest; there were 5 cases of papillary cancer and only one failed to show this characteristic. These results are consistent with the characterization of papillary carcinomas as hypervascular formulated by other authors.12 The resistance index, resistance expression or vascular impedance has to be taken into account, which suggests that, unlike in other organs,13 in the thyroid gland is not possible for vascular resistance parameters to be correlated with the type of neofromation.8 The fact of lower vascularization being found in papillary cancer might explain the low tendency towards hematogenous metastasis in this type of tumors, as well as their slow growth, given the direct relationship between angiogenesis and metastatic capacity.14 This is, according to the latest investigations on neovascularization,15 owing to the fact that by presenting less vessels, there would be less possibility of bloodstream invasion. This fact could be attributed to the extremely low production of angiogenic factors,16 which are responsible for the formation of tumor vessels, which in turn enable neofromation uncontrolled growth,17 since tumors without neovascularization have been experimentally shown not to grow beyond 1 or 2 mm.18

Histological types were consistent with those recorded in other studies, such as the one by Rivera Moscoso; follicular cancer was the most common. As for study sensitivity, it was very low, as we expected, but in comparison with other investigations it was similar.19 Specificity was also very similar to that found in the literature.7 Apparently, the diagnostic imaging method is not too useful for diagnosis, but it is to guide the direction the studies should be continued to.

It would remain for further investigations to verify whether there is a relationship between sparse vascularization in papillary carcinomas and possible low histological quantification of neoformed vessels, although there are authors that have failed to find any correlation between Doppler-obtained signals and vascular density.5 We believe these results may constitute one more step towards differentiation between malignant and benign nature in thyroid nodules, always supported by the rest of differential characteristics such as vascularity, contours, hypoechoic microcalcifications and content, having in mind the current impossibility for FNPA-obtained information to be substituted by a non-invasive method.19

References