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Malignancy of a Thyroid Nodule Can Be Predicted by Ultrasonography if It Has Microcalcifications and Is Solid and Larger than 2 cm

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Smith-Bindman R, Lebda P, Feldstein VA, Sellami D, Goldstein RB, Brasic N, Jin C, Kornak J. Risk of thyroid cancer based on thyroid ultrasound imaging characteristics: results of a population-based study. JAMA Intern Med. August 26, 2013. [Epub ahead of print]. doi: 10.1001/jamainternmed.2013.9245.

SUMMARY

Background

Ultrasound imaging is a principal tool for selecting thyroid nodules for FNA biopsy in order to determine whether a nodule is benign or malignant. Choosing which nodules are worthy of biopsy based on ultrasound characteristics is especially important, and there is a vast literature on this topic. The purpose of this study was to identify the ultrasound imaging characteristics associated with malignant nodules in order to create a standardized system for predicting the risk of cancer in a thyroid nodule.

Methods

The authors conducted a retrospective case–control study of consecutive patients who underwent ultrasound thyroid imaging between January 2000 and March 30, 2005. Thyroid cancers were verified through the California Cancer Registry. Cancers diagnosed through March 30, 2007, were included to allow a minimum of 2 years of follow-up. Patients diagnosed as having thyroid cancer were matched 4 to 1 with controls without cancer matched for age sex and year of ultrasound examination. The study included 96 patients with cancer and 369 controls. In 43 patients with cancer, a single nodule was identified by ultrasound and considered malignant. In 50 patients with cancer, multiple nodules were identified; consequently, one investigator reviewed all records to determine which nodules were malignant, but in a small (unspecified) number of nodules, this could not be done. Each ultrasound was reviewed independently by two radiologists, with good consensus on the readings.

Single predictor modeling was used to assess the association between specific ultrasound characteristics and cancer status using generalized estimating equations. The ultrasound variables that were statistically significant in this model were combined in various ways for a final multiple predictor model.

Results

A total of 8806 patients had 11,618 thyroid ultrasound exams during the study period; 105 cancers were diagnosed 1 day to 6 years after the ultrasound imaging. The incidence of thyroid cancer was 0.9 per 100 ultrasound exams. Thyroid nodules were found in 97% of patients with cancer and in 56% of controls.

Microcalcifications were found in 38.2% of cancer nodules versus 5.4% of benign nodules; the corresponding odds ratio (OR) was 11.6 (95% CI, 6.5 to 20.0). The odds for cancer increased with nodule size. Although coarse calcifications, nodule echogenicity, central vascularity, margins, and shape (more tall than wide) were also significantly associated with cancer in the single predictor analysis, the odds ratios were smaller, ranging from 1.6 to 2.9.

In the multiple predictor model, only three characteristics were significantly associated with the risk of cancer: microcalcification, size greater than 2 cm, and solid composition. If any one of these three characteristics was present, the sensitivity was 0.88 (95% CI, 0.80 to 0.94). If all three were present, the likelihood ratio was 28 (95% CI, 23 to 34), but the sensitivity was 0.07.

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Conclusions

Thyroid ultrasound imaging could be used to identify patients who have a low risk of cancer for whom biopsy could be deferred because they do not have any of the characteristics that predict malignancy.

ANALYSIS AND COMMENTARY

The authors claim that they have made a unique contribution by comparing the ultrasound characteristics of the cancer nodules with controls selected from a large number of patients without cancer. In both groups, there is purposely no data on FNA. The authors assert that other studies limited their analysis to patients who had biopsies based on the ultrasound examination, which led to ascertainment bias and overestimated the risk of cancer and the accuracy of ultrasound imaging. Unfortunately, this claim is difficult to accept. The authors show in tables of single predictor analysis that the usual ultrasound features of malignant nodules increase the odds ratio of malignancy: microcalcifications, solid, and larger than 2 cm. This last feature has been disputed (1). The multiple predictor model leads to discarding other features, such as coarse calcifications, more tall than wide, irregular borders, and increased intranodular vascularity, that have been found to be helpful as indicators of potential malignancy.

The authors cite the ATA guidelines as recommending FNA of nodules that are >0.5 cm, but this is erroneous (2). The revised guidelines recommend FNA of solid nodules >1 cm and nodules >0.5 cm only when they have suspicious sonographic features (2; Table 3).

Frates et al., in a consensus statement for the Society of Radiologists in Ultrasound in 2005 made reasonable recommendations with regard to which characteristics made nodules suspicious and worthy of FNA (3). Others have explored this area extensively with regard to diagnostic accuracy of various criteria for making a nodule suspicious for malignancy (4). There is agreement that cysts are not malignant, as found in this report. Perhaps the main contribution of the current article is that it will reopen the debate about whether it is worthwhile to perform FNA in nodules that are solid and 1 to 2 cm but without other criteria suggesting malignancy. In the commentary in the same issue of JAMA Internal Medicine as this article, Alexander and Cooper point out that hypoechoic, solid nodules larger than 1 to 1.5 cm with microcalcifications should be biopsied (5). Of course, these are likely to be papillary thyroid cancers. They also state that spongiform nodules as well as cysts need not be biopsied.

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