

Long-term follow-up of benign thyroid nodules shows favorable prognosis

March 3 2015

After five years of follow-up, a majority of asymptomatic, benign thyroid nodules exhibited no significant change in size, or actually decreased in size, and diagnoses of thyroid cancer were rare, according to a study in the March 3 issue of *JAMA*.

Detection of asymptomatic thyroid nodules has increased, largely from improved detection of small incidentally discovered nodules. Consensus is lacking regarding the optimal follow-up of cytologically (analysis of aspirated cells) proven benign lesions and sonographically (an imaging technique using ultrasonic waves) nonsuspicious nodules. Current guidelines recommend serial ultrasound examinations and repeat cytology exam if significant growth in the nodule is observed. However, little is known about the actual frequency and magnitude of nodule growth, and there is no reliable method for identifying patients likely to experience growth. The assumption that growing nodules increase a patient's risk of malignancy has been untested, according to background information in the article.

Sebastiano Filetti, M.D., of the Universita di Roma Sapienza, Rome, and colleagues studied the frequency, magnitude, and factors associated with changes in thyroid nodule size. The study involved 992 patients with 1 to 4 asymptomatic, sonographically or cytologically benign thyroid nodules. Patients were recruited from 8 hospital-based thyroid-disease referral centers in Italy between 2006 and 2008. Data collected during the first 5 years of follow-up, through January 2013, were analyzed.



Nodule growth occurred in 153 patients (15.4 percent). One hundred seventy-four of the 1,567 original nodules (11.1 percent) increased in size. Nodule growth was associated with presence of multiple nodules. In 184 individuals (18.5 percent), nodules shrank. Thyroid cancer was diagnosed in 5 original nodules (0.3 percent), only 2 of which had grown. New nodules developed in 93 patients (9.3 percent), with detection of one cancer.

"One of the goals of surveillance is the prompt detection and treatment of thyroid cancers that arise during follow-up or have been missed on the initial assessment. In the population we studied, these events were rare," the authors write.

"Only 2 of the 5 diagnoses of cancer in an established nodule were preceded by significant growth of the cancerous nodule. These data suggest that the American Thyroid Association's recommendation for indication for repeat cytology should be revised. Clinical and sonographic findings should probably play larger roles in the decision-making process."

In an accompanying editorial, Anne R. Cappola, M.D., Sc.M., and Susan J. Mandel, M.D., M.P.H., of the Perelman School of Medicine at the University of Pennsylvania, Philadelphia, (Dr. Cappola is also an Associate Editor, *JAMA*), write that this study has four important implications for the follow-up of thyroid nodules.

"First, these prospective data provide reassurance about the validity of a benign cytology result obtained by ultrasound-guided fine-needle aspiration and confirm a very low false-negative rate, at 1.1 percent. Second, the practice of routine sonographic surveillance with repeat fine-needle aspiration for growth, as recommended by published guidelines, is not the most efficient strategy to detect the very small number of missed cancers among previously sampled cytologically benign nodules.



The one-size-fits-all approach simply does not work. Instead, surveillance strategies should be individualized based on a nodule's sonographic appearance."

"Third, many nodules detected on ultrasound are small (i.e., "Thyroid nodules are pervasive, whereas <u>thyroid cancer</u> is not. The findings from Durante et al represent an important step in improving the efficiency and mitigating the expense of follow-up for the vast majority of <u>thyroid nodules</u> that are either cytologically or sonographically benign."

More information: DOI: 10.1001/jama.2015.0956 DOI: 10.1001/jama.2015.0836

Provided by The JAMA Network Journals

Citation: Long-term follow-up of benign thyroid nodules shows favorable prognosis (2015, March 3) retrieved 4 October 2023 from https://medicalxpress.com/news/2015-03-long-term-follow-up-benign-thyroid-nodules.html

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