

# Risk of Malignancy in Nonpalpable Thyroid Nodules: Predictive Value of Ultrasound and Color-Doppler Features

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The aim of the study was to correlate the sonographic [ultrasound (US)] and color-Doppler (CFD) findings with the results of US-guided fine needle aspiration biopsy (FNA) and of pathologic staging of resected carcinomas to establish: 1) the relative importance of US features as risk factors of malignancy; and 2) a cost-effective management of nonpalpable thyroid nodules.

Four hundred ninety-four consecutive patients with nonpalpable thyroid nodules (8–15 mm) were evaluated by US, CFD, and US-FNA. Ninety-two patients with inadequate cytology were excluded from the study. All patients with suspicious or malignant cytology underwent surgery, whereas subjects with benign cytology had clinical and US control 6 months later.

Thyroid malignancies were observed in 18 of 195 (9.2%) solitary thyroid nodules and in 13 of 207 (6.3%) multinodular goiters. Cancer prevalence was similar in nodules greater or smaller than 10 mm (9.1 vs. 7.0%). Extracapsular growth (pT<sub>4</sub>) was present in 35.5%, and nodal involvement in 19.4% of neoplastic lesions, with no significant differences between tu-

mors greater or smaller than 10 mm. At US cancers presented a solid hypoechoic appearance in 87% of cases, irregular or blurred margins in 77.4%, an intranodular vascular pattern in 74.2%, and microcalcifications in 29.0%.

Irregular margins (RR 16.83), intranodular vascular spots (RR 14.29), and microcalcifications (RR 4.97) were independent risk factors of malignancy. FNA performed on hypoechoic nodules with at least one risk factor was able to identify 87% of the cancers at the expense of cytological evaluation of 38.4% of nonpalpable lesions.

The majority of nonpalpable thyroid tumors can be identified by cytological evaluation of lesions presenting hypoechoic appearance in conjunction with one independent risk factor. Due to the nonnegligible prevalence of extracapsular growth and nodal metastasis, US-FNA should be performed on all 8–15 mm hypoechoic nodules with irregular margins, intranodular vascular spots or microcalcifications. Nonpalpable lesions of the thyroid without risk factors should be followed by means of clinical and US evaluation. (*J Clin Endocrinol Metab* 87: 1941–1946, 2002)

THE DISCOVERY RATE of nonpalpable thyroid nodules in the general population is increasing as a consequence of the widespread use of ultrasound (US) evaluation of the cervical region (1, 2). There is considerable controversy over whether clinically unapparent thyroid lesions should be assessed by fine needle aspiration biopsy (FNA) (3, 4). The conflicting attitudes are due to uncertainty about both the prevalence of malignancy in small thyroid lesions and the biological behavior of thyroid microcarcinomas (5–10), usually diagnosed retrospectively in resected goiters. Hence it has been suggested that, in the absence of previous neck irradiation or other identifiable risk factors, nonpalpable thyroid nodules not exceeding 10 or 15 mm in diameter should be managed only with neck palpation follow-up (3, 11).

Few prospective studies (12–15) have been addressed to the systematic evaluation of thyroid nodules incidentally discovered at sonography to correlate the dimensions and the US and color-Doppler (CFD) findings with the prevalence of cancer and its pathologic staging.

Abbreviations: CFD, Color-Doppler; FNA, fine needle aspiration biopsy; pT<sub>4</sub>, extracapsular growth; TNM, tumor size, nodal involvement and distant metastasis classification; US, ultrasound.

To determine optimal clinical management of nonpalpable thyroid nodules our study set out to correlate, in a prospective series, the findings of US and CFD examinations with the cytological and histological results so as to assess: 1) the prevalence of cancer; 2) the prevalence of malignancy in nodules greater or smaller than 10 mm, in solitary vs. multiple lesions and in dominant vs. nondominant lesions within multinodular goiters; 3) the relative risk of malignancy of the main US features (echogenicity, echo-structure, margins, vascular images, and microcalcifications); 4) the prevalence, on the basis of TNM stage, of aggressive behavior of the discovered thyroid cancers and the possibility of fixing a dimensional cut-off for the threat of extracapsular or metastatic growth; 5) cost-effective criteria for identifying which nonpalpable thyroid lesions should undergo FNA evaluation.

## Subjects and Methods

### Patients

Four hundred ninety-four consecutive patients (from 16 to 84 yr old, mean age: 47.8 ± 13.3 yr; males 64 and females 430) with nonpalpable thyroid nodules entered the prospective study between June 1995 and June 2000. Cases were selected from 3500 patients, referred to our thy-