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● *Original Contribution*

MANAGEMENT OF THYROID FOLLICULAR PROLIFERATION: AN ULTRASOUND-BASED MALIGNANCY SCORE TO OPT FOR SURGICAL OR CONSERVATIVE TREATMENT

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Abstract—This study was conducted to evaluate whether ultrasound characteristics of thyroid nodules with a known cytologic diagnosis of "follicular pattern" (indicative of follicular hyperplasia, follicular adenoma or follicular carcinoma) can be used to define a nodule malignancy score to limit surgery to selected, higher-risk cases. In pre-operative ultrasound results of patients diagnosed with a "follicular pattern" on cytology who subsequently underwent surgery, each nodule feature was given a score from 0 (most likely benign) to 2 (most likely malignant), resulting in a total score ranging from 0 to 11. The total nodule score (total malignancy score) was then compared with the definitive histologic diagnosis. According to our results, surgery is advisable in patients with score ≥4 (79% of carcinomas), ultrasound follow-up seems to be appropriate for patients with a score of 3 (21% of carcinomas) and no action is recommended for patients with score <3 (only benign nodules). (E-mail: giovanni.pompili@fastwebnet.it)

Key Words: **Diagnostic imaging, Ultrasound, Thyroid nodule, Follicular thyroid carcinoma, Cytodiagnosis, Fine-needle biopsy.**

INTRODUCTION

Thyroid nodules are common findings; the detection of non-palpable nodules using ultrasound (US) brings up the issue of good management of thyroid pathology (Rorive et al. 2010; Tae et al. 2007). The majority of thyroid nodules are benign. Malignant nodules are uncommon, representing only 5% of all nodules detected in the adult population and affecting mainly patients younger than 20 y or older than 60 y (Frates et al. 2005; Rorive et al. 2010; Tae et al. 2007).

Many ultrasound features of a thyroid nodule can be potential predictors of malignancy: a suspicious nodule is more commonly single, hypoechoic and solid and can exhibit a discontinued halo, irregular margins, microcalcifications and predominantly intranodular color flow. Size is not an important feature leading to the suspicion of nodule malignancy, though an important increase in size over a fixed period (>20% in 6 mo) has been defined by some authors as a predictor of malignancy (Frates et al. 2005; Tae et al. 2007). Diagnosis of malignancy cannot be based on ultrasound predictors only, and requires cytologic confirmation via fine-needle aspiration cytology (FNAC). At present, FNAC is considered the gold standard for primary diagnosis of benign and malignant nodules; it is usually diagnostic, with a sensitivity between 89% and 98% on an adequate sample (Pinchot et al. 2009). However, FNAC is not able to distinguish benign from malignant follicular lesions (Faquin 2009). In cytology, the term *follicular pattern* can indicate three different final diagnoses: follicular hyperplasia, follicular adenoma and follicular carcinoma.

Currently, all patients with a cytologic diagnosis of follicular pattern undergo partial or total thyroidectomy; this means, for example, that a patient with hyperplasia, a very common benign condition, in the presence of a cytologic diagnosis of follicular pattern is referred to surgery.

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The aim of this study was to devise an ultrasound-based score reliably predicting the benign or malignant nature of the nodule, after cytologic diagnosis of follicular pattern.

METHODS

Patients

All patients entered into this retrospective study signed an informed consent before each invasive diagnostic (*e.g.,* FNAC) or surgical procedure. No consent was required for the diagnostic ultrasound (US). For this study, patients' data were anonymized, and individual patients were identified exclusively by a number, so that no sensitive data were used. This retrospective study was approved by the local ethics committee.

All patients with a cytologic diagnosis of follicular pattern who underwent thyroidectomy at our university hospital between January 1998 and December 2009 were identified, for a total of 127 patients. Nineteen of the 127 identified patients were then excluded because of incomplete data. Therefore, 108 patients were analyzed by comparing the results of their pre-operative US examination with the results of histologic analysis on the surgically resected specimen. After this analysis, 6 additional patients were excluded because their histologic diagnosis was papillary microcarcinoma, which is undetectable with common imaging techniques. Thus, the final study population consisted of 102 patients (80 females and 22 males; age range, 15–81 y; age (mean ± standard deviation), 46 ± 14 y).

Image analysis

Pre-operative US examinations were performed by two board-certified radiologists (G.P., Nicola Flor), with more than 10 y of experience in neck ultrasound imaging, using different ultrasound devices along with dedicated linear small part probes, with a frequency ranging from 7 to 14 MHz. A pulse repetition frequency of 2400 Hz and a color gain of 40%–50% were used for the Doppler US, performed with a linear high-frequency probe (7.5–10 MHz). Each examination was performed by a single radiologist and the relevant report (written by that same radiologist soon after the end of the examination), along with corresponding images, underwent a consensus review by two of the authors, who collected data on number, size and features of the nodules identified. All FNACs were done by two board-certified radiologists (G.P., Nicola Flor), who performed the aspiration under US guidance, and a pathologist, who used an Ultrafast Papanicolaou stain to make a quick assessment of the adequacy of the sample (*i.e.,* presence in the sample of enough thyroid cells to make a diagnosis). Aspirations were performed with either 23- or 25-gauge needles, 10 cm long, first by capillarity and eventually by forced syringe suction. The most commonly used stains for diagnosis were Papanicolaou and hematoxylin and eosin. One to three aspirations were performed on the suspicious nodule, as determined by the pathologist; if the patient had more than one nodule, FNAC was performed on the nodule that looked more suspicious at the US examination.

Table 1. Description of the proposed score system on the basis of nodule characteristics

Nodule characteristic	Ultrasound malignancy score		
	0	1	2
Number	Many	—	Single
Margins	Regular	—	Irregular
Color flow	Perinodular	Peri-intranodular	Intranodular
Structure	Colloidal	Solid	—
Echogenicity	An-/iso-/hyperechoic	Hypoechoic	—
Halo	Continuous	Discontinuous	—
Calcifications	Macro-calcifications	Micro-calcifications	—
Growth	—	>20% in 6 mo	—

On the basis of the data collated from the review of the pre-operative US reports and images, a score from 0 (most likely benign) to 2 (most likely malignant) was assigned to the following US features of the suspicious nodules examined: number, margins, color flow, structure, echogenicity, halo, calcifications, growth (Table 1). Individual features scores were summed to obtain a total malignancy score (TMS) for the nodule, ranging from 0 to 11. One point was assigned for the presence of each of the following US malignant features: solid structure, hypoechoic pattern, discontinuous halo, mixed (both perinodular and intranodular) color flow, micro-calcifications, growth ≥20% in 6 mo. Two points were assigned to the presence of irregular margins and of predominantly intranodular color flow, these features being extremely uncommon in benign nodules. Two

Table 2. Distribution of ultrasound features considered predictive of malignant disease by histologic diagnosis

Ultrasound nodule feature	Histologic diagnosis			
	Hyperplasia (n = 42)	Adenoma (n = 46)	Carcinoma (n = 14)	Total (n = 102)
Single	14 (33%)*	30 (65%)	12 (86%)	56 (55%)
Irregular margins	2 (5%)	2 (4%)	6 (43%)	10 (10%)
Intranodular color flow	0	3 (7%)	2 (14%)	5 (5%)
Solid	35 (83%)	42 (91%)	13 (93%)	90 (88%)
Hypoechoic	10 (24%)	20 (43%)	12 (86%)	42 (41%)
Discontinuous halo	1 (2%)	5 (11%)	8 (57%)	14 (14%)
Micro-calcifications	1 (2%)	1 (2%)	1 (7%)	3 (3%)
Growth >20% in 6 mo	6 (14%)	4 (9%)	0	10 (10%)

* Number (%).