

Role of conventional ultrasonography and color flow-doppler sonography in predicting malignancy in 'cold' thyroid nodules

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Abstract

The aim of the present study was to establish the usefulness of conventional thyroid ultrasonography (US) and color flow-doppler (CFD) sonography in the assessment of 'cold' thyroid nodules. One hundred and four consecutive patients with thyroid nodules who were to undergo surgery were examined by US and CFD before thyroidectomy. Conventional US evaluated the presence of a halo sign, hypoechogenicity and microcalcifications. The vascular pattern on CFD was classified as follows: Type I, absence of blood flow; Type II, perinodular blood flow; Type III, marked intranodular blood flow. On histology, 30 nodules were diagnosed as malignant (carcinoma, CA) and 74 as benign nodules (BN). On US, the echographic pattern most predictive for malignancy was absent halo sign, which was found in 20/30 CA and in 17/72 BN ($P = 0.0001$; specificity 77.0%; sensitivity 66.6%). The most specific combination on US, absent halo sign/microcalcifications, was found in 8/30 CA and in 5/74 BN ($P < 0.005$; specificity 93.2%, sensitivity 26.6%). The Type III pattern on CFD was found in 20/30 CA and 38/74 BN (not statistically significant). The combination of absent halo sign on US with Type III pattern on CFD was found in 15/30 CA and in 8/74 BN ($P < 0.0001$; specificity 89.0%, sensitivity 50.0%). The combination of absent halo sign/microcalcifications on US with Type III pattern on CFD was the most specific combination of the two techniques, being found in 5/30 CA and in only 2/74 BN ($P < 0.01$; specificity 97.2%, sensitivity 16.6%).

In conclusion, findings on US and CFD become highly predictive for malignancy only when multiple signs are simultaneously present in a thyroid nodule. Thus the predictive value of these techniques increases at the expense of their sensitivity. Only in a small proportion of patients with thyroid carcinoma is US and CFD information highly predictive of malignancy.

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Introduction

Thyroid nodules are a common finding in the general population living in iodine sufficient areas; their prevalence dramatically increasing in areas of iodine deficiency (1, 2). The great majority of thyroid nodules are benign nodules (BN), less than 5% of them being malignant (carcinomas, CA) (3–5). While cytological examination of fine needle aspirates (FNAC), due to its high sensitivity and specificity, is the best single test for discriminating malignant thyroid nodules, (6–10) several studies have been performed to establish the ability of thyroid ultrasonography (US) to differentiate benign from malignant thyroid nodules. Indeed, compared with FNAC, thyroid US has the advantage of being a non-invasive procedure and giving immediate information. Among several US patterns, hypoechogenicity of the nodule, microcalcifications and absence of halo sign were reported to be useful in predicting thyroid malignancy (11–13).

The availability of color flow-doppler (CFD) sonography allows the evaluation of nodular and perinodular blood

flow. The usefulness of this technique in predicting malignancy of thyroid nodules is still controversial (14–18). The aim of this study was to assess the ability of conventional thyroid US and CFD sonography, either alone or in combination, to predict malignancy of thyroid 'cold' nodules.

Materials and methods

Patients

The study included 104 consecutive patients, 70 females (mean age 39.1 ± 15 years, range 15–74 years) and 34 males (mean age 48.8 ± 13.9 years, range 9–71 years), with a single thyroid nodule, either in a normal thyroid (65 patients) or in a goiter (39 patients), and who underwent surgery for compressive symptoms or clinical suspicion of malignancy. All the nodules were 'cold' on ^{99m}Tc scintiscans and patients were euthyroid, as assessed by the measurement of serum thyroid-stimulating hormone and free thyroid hormones.

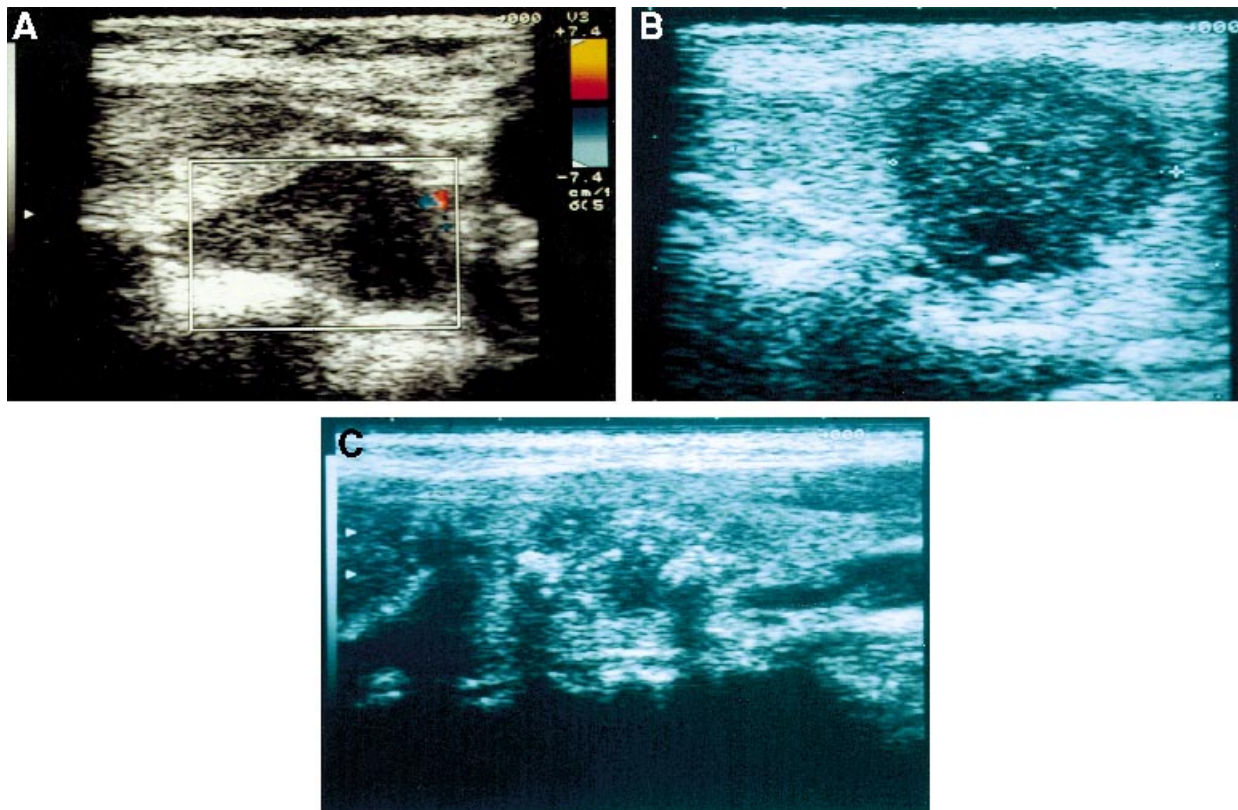


Figure 1 Conventional echographic patterns. A: absence of halo sign in sporadic medullary carcinoma (longitudinal section). B: hypoechogenicity in papillary thyroid carcinoma (longitudinal section). C: intranodular calcification, absence of halo sign and hypoechogenicity are also present in papillary thyroid carcinoma (longitudinal section).

Conventional and CFD sonography

Conventional US and CFD sonography were performed using a color doppler apparatus (AU 590 Asynchronous, Esaote Biomedica, Firenze, Italy), with a 7.5 MHz linear transducer. Data were collected blindly by two independent examiners (T R and S M). When results of the examiners were discordant, agreement was found by conjoint re-examination of the patient. Conventional US evaluated: (i) the echogenicity of the nodule with respect to the surrounding thyroid parenchyma; (ii) the presence of halo sign (transonic rim surrounding the lesion); and (iii) the presence of microcalcifications defined as hyperechoic spots less than 2 mm with acoustic shadowing. CFD evaluated the presence and the pattern of blood flow: Type I, absence of blood flow; Type II, perinodular and absent or slight intranodular blood flow; and Type III, marked intranodular and absent or slight perinodular blood flow (Figs 1 and 2).

Statistical evaluation was performed using the chi-square test, and the predictivity test of Galen and Gambino (19).

Results

Histological examination demonstrated CA in 30 nodules: 18 papillary carcinomas, 6 medullary carcinomas, 5 follicular carcinomas and 1 thyroid lymphoma. Seventy-four nodules were benign with the following histological pattern: 43 micro-macrofollicular, 18 microfollicular, 11 macrofollicular, and 2 Hurtle cell adenoma (Table 1). The size of malignant nodules was 4.2 ± 5.7 ml (range 0.2–25); the size of BN was 11.5 ± 13.4 ml (range 0.2–60).

Conventional US

US patterns considered were: (i) absence of halo sign; (ii) microcalcifications; and (iii) hypoechogenicity. The single US pattern that was most predictive of malignancy (Table 2) was absent halo sign ($P < 0.0001$; specificity 77.0%, sensitivity 66.6%). Absent halo sign/microcalcifications was the most specific double combination of US patterns ($P < 0.005$; specificity 93.2%, sensitivity 26.6%). When all the three patterns were considered together, no gain in specificity was obtained.

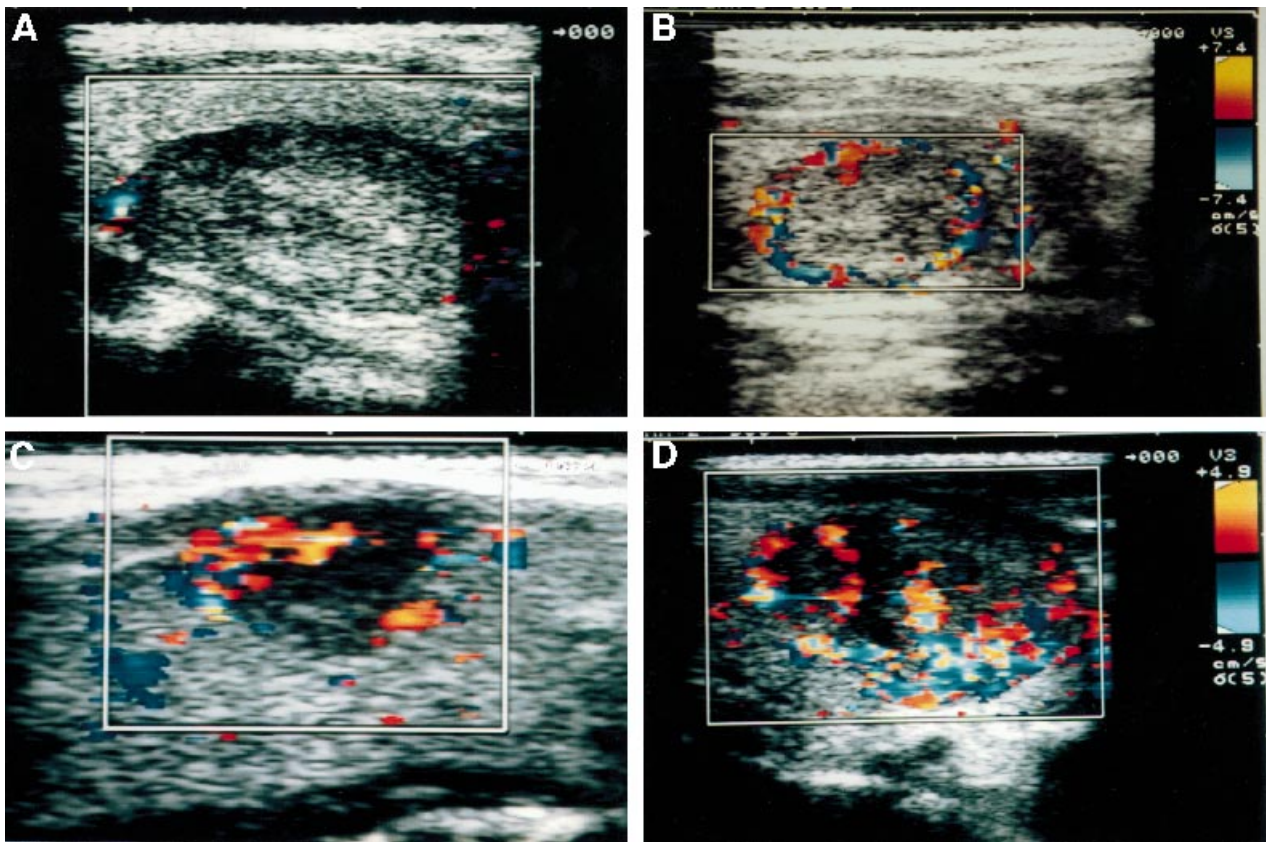


Figure 2 Color flow-doppler sonographic patterns. A: absence of blood flow (Type I). B: perinodular blood flow (Type II). C: slight intranodular blood flow (Type III). D: marked intranodular blood flow (Type III).

CFD sonography

The CFD pattern was Type I in 23 nodules, Type II in 23, and Type III in 58 (Table 3). In particular, an intranodular vascularization was found in 20/30 CA, but also in 38/74 BN (not statistically significant).

Combination of conventional US and CFD sonography

For all US features, the combination with Type III pattern on CFD increased the specificity but reduced the sensitivity in predicting CA (Table 4). The most specific double combination of US with Type III on CFD was absent halo sign/microcalcifications ($P < 0.01$; specificity 97.2%, sensitivity 16.6%).

Discussion

The absence of halo surrounding the nodule was the pattern most predictive for malignancy on conventional US. This sign was found in 66.6% CA and in 22.9% BN. The sensitivity (66.6%) and specificity (77.0%) of this sign was higher than in other reports (12). The finding of intranodular microcalcifications had lower

sensitivity (50.0%) and specificity (75.6%) than the absence of halo sign, similar to what has been observed by other authors (12, 20–23). A hypoechoic aspect was found in 66.6% CA and in 51.3% BN, in agreement with the observations of Solbiati *et al.* (13) and Takashima *et al.* (12). Hypoechoogenicity, absence of halo sign and microcalcifications have already been reported as single patterns suggestive of malignant thyroid nodules in previous studies (7, 23–26). A solid nodule, with a hypoechoic aspect and irregular borders was regarded as CA in most of the reports that considered also combinations of several patterns (25–28). However, some of these studies were inhomogeneous for patient selection since 'hot' thyroid nodules were also included.

Table 1 Histological pattern in thyroid nodules.

Carcinoma (n = 30)		Benign nodule (n = 74)	
Type	No.	Type	No.
Papillary	18	Micro-macrofollicular	43
Medullary	6	Microfollicular adenoma	18
Follicular	5	Macrofollicular	11
Lymphoma	1	Hurtle adenoma	2

Table 2 Conventional ultrasonographic patterns and histology in thyroid nodules.

Echographic pattern	Carcinoma	Benign nodules	Significance	Specificity (%)	Sensitivity (%)	Positive predictive value (%)	Negative predictive value (%)
Absent halo sign	20/30	17/74	$\chi^2 = 17.7$ $P < 0.0001$	77.0	66.6	54.0	85.0
Microcalcifications	13/30	18/74	$\chi^2 = 3.68$ $P < 0.05$	75.6	54.0	55.6	76.7
Hypoechoogenicity	20/30	38/74	$\chi^2 = 2.00$ $P < 0.15$	48.6	66.6	34.4	78.2
Absent halo sign + hypoechoogenicity	18/30	13/74	$\chi^2 = 18.0$ $P < 0.0001$	82.4	66.0	58.0	83.5
Absent halo sign + microcalcifications	8/30	5/74	$\chi^2 = 7.70$ $P < 0.005$	93.2	26.6	61.5	75.8
Hypoechoogenicity + microcalcifications	9/30	15/74	$\chi^2 = 1.13$ $P < 0.28$	79.7	30.0	26.4	73.7

Table 3 Color flow-doppler (CFD) sonography and histological pattern in thyroid nodules.

CFD pattern	Carcinoma	Benign nodules	Significance	Specificity (%)	Sensitivity (%)	Positive predictive value (%)	Negative predictive value (%)
Type I absence of blood flow	5/30	18/74	$\chi^2 = 0.70$ $P = 0.39$	75.6	16.6	21.7	69.0
Type II perinodular blood flow	5/30	18/74	$\chi^2 = 0.70$ $P = 0.39$	75.6	16.6	25.0	65.0
Type III intranodular blood flow	20/30	38/74	$\chi^2 = 2.03$ $P = 0.15$	48.6	66.6	34.4	78.2

Table 4 Combination of conventional ultrasonography and color flow-doppler sonography (CFD) in thyroid nodules.

Echographic pattern/ CFD	Carcinoma	Benign nodules	Significance	Specificity (%)	Sensitivity (%)	Positive predictive value (%)	Negative predictive value (%)
Absent halo sign/ Type III	15/30	8/74	$\chi^2 = 19.0$ $P < 0.0001$	89.0	50.0	65.2	81.4
Microcalcifications/ Type III	7/30	10/74	$\chi^2 = 1.50$ $P < 0.20$	86.4	23.3	41.1	73.5
Hypoechoogenicity/ Type III	14/30	22/74	$\chi^2 = 2.70$ $P = 0.10$	70.2	44.0	38.8	76.4
Absent halo sign + microcalcifications/ Type III	5/30	2/74	$\chi^2 = 6.30$ $P < 0.01$	97.2	16.6	71.1	74.2
Absent halo sign + hypoechoogenicity/ Type III	13/30	6/74	$\chi^2 = 17.7$ $P < 0.0001$	91.8	43.3	68.4	80.0
Hypoechoogenicity + microcalcifications/ Type III	6/30	8/74	$\chi^2 = 1.50$ $P = 0.20$	89.1	20.0	42.8	73.3

In the present investigation only 'cold' thyroid nodules on scintiscans were included, and the predictive value of two or more combined echographic patterns was evaluated. We found that the most predictive combination on conventional US was absence of halo sign plus microcalcifications. This combination had a high specificity (93.0%), but a low sensitivity (36.0%). The predictive value of other combinations was even lower.

Intranodular blood flow on CFD was found in 66.6% of carcinomas and in 51.3% of BN. Thus the predictive value of CFD alone was poor, in agreement with data reported by Fobbe *et al.* (15) and Solbiati *et al.* (25). Other authors (29) suggested that carcinoma and autonomous adenoma can be excluded in patients with nodular goiter when normal vascularization is demonstrated. In contrast, others (14, 30) did not find a correlation between the presence of specific color signals and pathology, as the detection of color signals was dependent on the size of the nodule rather than on its histology. On the other hand, Anguissola *et al.* (18) as well as other authors (15–17, 28–34) reported that an increased nodular blood flow was associated with thyroid carcinoma. In our series, we evaluated the combination of each pattern on conventional US with an intranodular blood flow on CFD. Absence of halo sign plus microcalcifications on US combined with intranodular blood flow on CFD was found to be highly specific for malignancy, being seen in only 2/74 BN. Unfortunately it was present in only 5/30 carcinomas. Thus, the gain in specificity (97.2%) occurred at the expense of sensitivity.

In summary, we confirm that taken by itself no single pattern on US and CFD is highly predictive for malignancy in 'cold' thyroid nodules. The combination of patterns that are more frequently associated with malignancy are the absence of halo sign and microcalcifications. An intranodular blood flow on CFD only slightly increased the predictivity of signs observed on conventional US.

In conclusion, findings on US and CFD become highly predictive for malignancy only when multiple signs are simultaneously present in a thyroid nodule. However, the predictive value of these techniques increases at the expense of their sensitivity. Thus in less than 20% of patients with CA can malignancy be predicted with high specificity by US and CFD sonography.

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