Absence of central vascularization in papillary thyroid microcarcinoma on color Doppler

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ABSTRACT

Objective. To evaluate the possible diagnostic relevance of the intratumoral vascularity of papillary thyroid microcarcinoma.

Method. This was a retrospective study in which color Doppler sonographic examinations of 30 cases of papillary thyroid carcinoma diagnosed by fine needle aspiration and cytological examination were analyzed. Two groups were considered: microcarcinomas (≤ 1.0 cm) and larger nodules (> 1.0 cm).

Results. None of the microcarcinomas showed central vascularization, whereas 56% of the larger nodules presented this finding (p < 0.004). There was no central vascularization in any of the cases of papillary thyroid microcarcinoma evaluated.

Conclusion. The presence of central vascularization in nodules up to 1.0 cm probably does not indicate an increased risk of malignancy and should not be a definitive indication for cytological evaluation. However, absence of vascularization does not eliminate the risk of malignancy and, therefore, should not be a criterion for dismissing the need for puncture.

Key words. Thyroid; ultrasonography; neoplasms, diagnosis

RESUMO

Ausência de vascularização central no microcarcinoma papilar da tireoide ao Doppler colorido

Objetivo. Avaliar a possível relevância diagnóstica da vascularização intratumoral do microcarcinoma papilar da tireoide.

 Método. Estudo retrospectivo no qual os exames ultrasonográficos com Doppler colorido de 30 casos de carcinoma papilar da tireoide diagnosticados por punção com agulha fina e análise citopatológica foram analisados. Foram considerados dois grupos: microcarcinomas (≤ 1,0 cm) e macrocarcinomas (> 1,0 cm).

Resultados. Nenhum dos microcarcinomas exibiu vascularização central, e 56% dos nódulos maiores apresentaram tal achado (p < 0,004). Não foi verificada vascularização central em nenhum dos casos de microcarcinoma papilar da tireoide avaliados.
A presença de vascularização central em nódulos com até 1 cm provavelmente não indica maior risco de malignidade e não deve ser critério para indicação de avaliação citopatológica. Entretanto, a ausência de vascularização não elimina o risco de malignidade e, portanto, não deve ser critério para exclusão da necessidade de punção.

Palavras-chave. Tireoide; ultrassonografia; neoplasias; diagnóstico

INTRODUCTION

The incidence of thyroid cancer increased 2.4 times from 1973 through 2002 in the United States, but there was no significant change in the incidence of less common histological types such as follicular, medullary and anaplastic carcinomas. This increase was attributed to the higher (2.9 times) incidence of papillary carcinoma; 49% of these consisted of tumors measuring 1.0 cm or less. In addition, mortality due to thyroid cancer remained stable during the study period, suggesting that there was increased detection of subclinical tumors and not a true increase in disease occurrence over time. The more frequent use of ultrasound and fine-needle puncture for cytological diagnosis played a major role in this process. These findings appear to be similar to the reality found in Brazil. Nevertheless, there was a reduction in the incidence of follicular carcinoma, which is probably related to the introduction of iodized salt in food.

Thyroid carcinomas measuring up to 1.0 cm are called microcarcinomas and are almost exclusively of the papillary type. They account for about 40% of all cases according to reviews of histopathological findings of thyroidectomy, including incidental cases. It is difficult to predict aggressiveness at diagnosis, since lymph node metastasis are not infrequent and rare cases of distant metastasis and deaths have been described.

Color Doppler is available in current ultrasound devices. It allows the noninvasive evaluation of tissue vascularity. It is controversial whether there is increased vascularity of malignant thyroid nodules on color Doppler. In a recent study, we verified a significant percentage of cases of papillary carcinoma without central vascularization. However, in this study and in several others, a correlation between vascularity and size of the nodules was not established.

The definition of the characteristics of suspicious thyroid nodules measuring up to 1.0 cm is of great importance, given that the main selection criterion for puncture and cytological evaluation accepted by endocrinology and radiology societies is size (>1.0 cm). The objective of the present study is to assess the relevance of central vascularization in papillary thyroid microcarcinomas.

METHOD

This was a retrospective study in which 30 consecutive cases of papillary thyroid carcinoma diagnosed between February 2010 and February 2012 at Centro de Diagnóstico por Imagem Ltda., Brasília (DF) were evaluated.

The cases were retrospectively selected from patient files. They necessarily included an evaluation of B-mode ultrasound and color Doppler examination, measurement of the major axis of the nodules and a conclusive cytopathologic report of papillary thyroid carcinoma. B-mode ultrasound and color Doppler examinations were done using Toshiba equipment model Xario XV (SSA 660A), with a high-resolution linear transducer (14 MHz). The study with color Doppler had its parameters adjusted for each case, and Power Doppler was also used.

We evaluated the vascularity of a series of cases of papillary thyroid carcinoma considering two subgroups: microcarcinomas (nodules smaller than or equal to 1.0 cm) and nodules larger than 1.0 cm (macrocarcinomas).

Fine-needle puncture was performed with a free-hand non-aspiration technique, with the aid of an ultrasound device, without anesthesia, using a 30x0.7 mm (22G) needle, and the number of punctures (up to three) varied depending on the quality and quantity of the material obtained.
The ultrasound study and the punctures were performed by one of the authors (MASF).

The cytopathological analyzes were conducted in two laboratories in Brasilia, DF, which prepared the slides using hematoxylin and eosin stain (HE).

The data obtained were organized and analyzed using Excel 2010 (Microsoft) and STATDISK 11.1.0 (Pearson Education). We used the chi-square statistical analysis and \( p \leq 0.05 \) was considered statistically significant.

The study protocol was approved by the Ethics Committee of the School of Medicine, University of Brasilia. Participants did not have to sign an informed consent form because this was a retrospective study based on patient files.

RESULTS

Thirty thyroid nodules diagnosed as papillary carcinoma were studied. There were 23 (77%) women and 7 (23%) men with a mean age of 43 years and range of 17-70 years.

The average size of the nodules was \( 1.27 \pm 0.77 \) cm (0.5 to 4.3 cm). There were 12 (40%) microcarcinomas and 18 (60%) macrocarcinomas. However, two cases were excluded from each group due to the presence of extensive internal microcalcifications in nodules that determined twinkling artifacts, which prevented evaluation with color Doppler.

As shown in table 1, the presence of central vascularization was found in only 35% (9/26) of the nodules and all of them were larger than 1 cm, which corresponded to 56% of these (9/16). The ten microcarcinomas analyzed on color Doppler did not show central vascularization. The difference between groups was statistically significant (\( p < 0.004 \)).

In table 2, it is observed that microcalcifications were present in 57% (17/30) of the nodules. Microcarcinomas had the highest percentage of microcalcifications (75%). Macrocarcinomas had a greater absence rate of microcalcifications (66%), but this difference was not significant (\( p = 0.09 \)).

DISCUSSION

Most societies of endocrinology and radiology consider size > 1.0 cm and sonographic characteristics as criteria for the selection of thyroid nodules that should be punctured. Several sonographic features have been associated with a higher probability of malignancy, such as increased intranodular vascularity, microcalcifications, hypoechogeticity, irregular margins, absence of halo and prevalent anteroposterior diameter, but these findings are not sufficient to identify all malignant nodules.\(^{15-17}\)

Nodules smaller than 1.0 cm should be evaluated in the presence of suspicious ultrasonographic characteristics and, possibly, when family history of papillary carcinoma, cervical radiotherapy, ionizing radiation exposure, partial thyroidectomy prior to diagnosis of papillary carcinoma or increased metabolic activity in PET-CT scans are observed.\(^{15-17}\)

Cytological examination of the material obtained by fine needle aspiration (FNA) of thyroid nodules is the gold standard to differentiate between benign

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**Table 1. Presence of central vascularization in papillary thyroid carcinomas on color Doppler**

<table>
<thead>
<tr>
<th>CENTRAL VASCULARIZATION (%)</th>
<th>WITH</th>
<th>WITHOUT</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macrocarcinomas</td>
<td>9 (56)</td>
<td>7 (44)</td>
<td>16 (100)</td>
</tr>
<tr>
<td>Microcarcinomas</td>
<td>0 (0)*</td>
<td>10 (100)</td>
<td>10 (100)</td>
</tr>
<tr>
<td>Total</td>
<td>9 (35)</td>
<td>17 (65)</td>
<td>26 (100)</td>
</tr>
</tbody>
</table>

*p < 0.004

**Table 2. Presence of microcalcifications in papillary thyroid carcinomas on ultrasound**

<table>
<thead>
<tr>
<th>MICROCALCIFICATIONS (%)</th>
<th>WITH</th>
<th>WITHOUT</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microcarcinomas</td>
<td>9 (75)</td>
<td>3 (25)</td>
<td>12 (100)</td>
</tr>
<tr>
<td>Macrocarcinomas</td>
<td>8 (44)</td>
<td>10 (56)</td>
<td>18 (100)</td>
</tr>
<tr>
<td>Total (n = 30)</td>
<td>17 (57)</td>
<td>13 (43)</td>
<td>30 (100)</td>
</tr>
</tbody>
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and malignant nodules for surgical treatment.\textsuperscript{10-18} Since thyroid ultrasound is noninvasive, without contraindication and easy to perform, there is a concern to define ultrasound parameters that can differentiate benign from and malignant nodules and that could dismiss the need for biopsy. For example, a thyroid ultrasound risk score (TRUS) that takes into account the solid eco-structure, irregular margins and hypoehogenicity of the nodule was recently designed. But despite the fact that sensitivity was higher than that of other scores, it was insufficient to identify nodules that would not need to be investigated by fine-needle aspiration.\textsuperscript{18}

A classification based on the vascularity of thyroid nodules on color Doppler that would be associated with the risk of malignancy has been suggested.\textsuperscript{14} However, poorly vascularized malignant nodules and benign hypervascular nodules are frequently reported, but there is often no correlation with their size and histological type.\textsuperscript{8-13}

In the present study, only 35\% (9/26) of the papillary carcinomas had central vascularization, and all were found in macrocarcinomas. Seven (44\%) of these nodules did not have central vascularization. In addition, none (0/10) of the microcarcinomas showed central vascularization (Figure 1 A-D). In four cases, the presence of extensive internal microcalcifications in nodules determined technical twinkling artifacts\textsuperscript{19} that prevented color Doppler evaluation (figure 1 E-F). Therefore, they were excluded from the analysis. Such artifacts can be a cause of error in exams and can be confused with extensive vascularization.

Figure 1: (A) Hypoechoic nodule with microcalcifications, measuring 0.6 cm, showing only peripheral vascularization on Power Doppler (B). (C) Hypoechoic nodule, with irregular contour and macrocalcifications, measuring 2.2 cm, showing predominant central vascularization on color Doppler (D). (E) Hypoechoic nodule with extensive microcalcifications, measuring 1.0 cm, with impaired analysis of vascularization on color Doppler (F) due to extensive twinkling artifacts.
Therefore, central vascularization could be exclusive of nodules larger than 1.0 cm. In a study that proposed the classification of thyroid nodule vascularization on color Doppler that correlated with the risk of malignancy, thirteen cases of malignant nodules were described, of which only two measured 1.0 cm; all the other nodules were larger, with an average of 3.88 cm. This could justify the inadequacy of the study findings to microcarcinomas.

A study of 197 malignant thyroid nodules measuring up to 1.0 cm showed central vascularization in only 9% of them. The authors concluded that intranodular vascularization was not useful to differentiate between benign and malignant nodules, being more frequent in benign nodules, but without statistical significance. The frequent fibrosis within papillary carcinomas could explain the low prevalence of vascularization in smaller nodules. With the growth of tumors, cell proliferation would make vascularization more frequent. In a study that evaluated the classifications by Lagalla et al. and Chammas et al., we observed that internal vascularization of benign thyroid nodules is common, which could make the use of color Doppler imaging difficult for the stratification of malignancy risk.

In a study that analyzed 34 malignant and 36 benign thyroid nodules using ultrasound and color Doppler, it was noted that the presence of microcalcifications was the only statistically significant criterion on which increased suspicion of malignancy was based. This is consistent with the observation that hypoechoic thyroid nodules with microcalcifications show a high probability of being papillary carcinomas. Microcalcifications were observed in 75% of the microcarcinomas in the present study, and in one case it was the only finding in apparently isoechoic nodules that were not delimited. However, there was no significant difference in the presence of microcalcifications in relation to the size of the nodules.

Although the treatment and natural history of papillary thyroid microcarcinoma are controversial, presence of cervical metastasis is not frequent and aggressiveness of tumors cannot be predicted exclusively by the size of the nodules. The recommendations of scientific societies that suggest that only nodules with more than 1.0 cm be punctured, regardless of their characteristics, can be questioned. Thyroid nodules measuring up to 1.0 cm with suspicious characteristics, such as irregular contour, hypoechoigenicity and microcalcifications, should be punctured for cytological evaluation, regardless of color Doppler vascularity, since these nodules usually do not show central vascular flow. The presence of internal vascularity may be relevant for larger nodules.

The diagnosis of papillary thyroid carcinoma was established by cytological examination of material obtained by FNA, which has been described to be of excellent reliability.

In conclusion, the presence of central vascularization on color Doppler was not observed in any of the nodules of papillary thyroid microcarcinomas described. The presence of central vascularization in nodules measuring up to 1.0 cm probably does not indicate increased risk of malignancy and should not be a criterion for cytopathological evaluation. On the other hand, absence of vascularization does not eliminate the risk of malignancy and should not be a criterion to dismiss the need for puncture.

REFERENCES

Clinical behavior and outcome of papillary thyroid cancers smaller than 1.5 cm in diameter: study of 299 cases. J Clin Endocrinol Metab. 2004;89(3):311-5.


