

Do Intranodular Macrocalcifications Really Play an Important Role in Sonographic Prediction of Malignancy?

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The Original research article, written by Park, et al.¹ entitled, “Thyroid Nodules with Macrocalcification: Sonographic Findings Predictive of Malignancy.” in the March-2014 issue of YMJ, is a well-written paper and we want to acknowledge Park, et al.¹ for their comprehensive article on malignant thyroid nodules with macrocalcification as it provides important informations with which to potentially diagnose malignant thyroid nodules.

Nevertheless, we would like to discuss a few points of emphasis on the general profile of thyroid nodules and their calcifications, especially the description and analysis of macrocalcification and rims of soft tissue around calcified zones.

In this paper, the authors reported that echogenic foci of calcification larger than 1 mm at the longest diameter were considered as representative of macrocalcifications, that bright echoes of less than 1 mm with or without acoustic shadowing were accepted as microcalcification and that combination of micro-macrocalcifications in a nodule was classified as a nodule with microcalcification and excluded from the study. However, we believe that, utilizing a thin slight borderzone with a threshold size of 1 mm to distinguish between micro and macrocalcifications can create serious bias in the statistical analysis and would definitely affect the results of the research, especially the sensitivity and positive predictive values (PPV) for sonography in differentiating between malignant and benign nodules, according to intranodular calcification size.

In previous reports, generally, 2 mm was considered as the cut-off value between micro and macrocalcifications, in which bright and granular calcifications ≤ 2 mm in diameter, with or without acoustic shadows, were considered to be microcalcifications; meanwhile calcifications with a maximum diameter >2 mm, including lumpy, irregular, peripheral, eggshell and coarse calcifications, were defined as macrocalcifications.^{2,3} As no data on the size, nature, and number of nodules and macrocalcification patterns were given, we have serious suspicions about the accuracy of the results of this original research. We believe that the authors took the threshold value of 1 mm for distinguishing benign and malignant nodules in order to perform a diagnostic fine-needle aspiration biopsy (FNAB) and to avoid having inadequate sampling of FNAB-cytology due to larger calcifications; the authors reported a high rate of unsuccessful biopsy sampling in nodules with macrocalcification (21%). Such non-diagnostic cytology would also limit the efficacy of sonography in predicting the malignant nature of such nodules.

Like the calcification widths, existence of a 1 mm or larger soft tissue rim circumscribing macrocalcification was also defined as soft tissue echogenicity and

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the authors reported that a soft tissue rim is significantly associated with malignancy which is also doubtful, based on our experience. Furthermore, the results of the research revealed, as seen in Table 3- that the presence of a soft-tissue rim predicts malignancy with a specificity of 23.6%, PPV of 31.5% and an accuracy of 42.5. Accordingly, the aforementioned soft-tissue echogenicity could easily represent false-negative malignancies for the statistics and results of the research.

As written in the text, there was one case of follicular carcinoma and 389 cases of follicular adenomas in the study group and no surgical proof was given for sonographically benign-appearing nodules, another entity that might lead to over and misdiagnosis of nodules with macrocalcification. In our experience, follicular adenomas and carcinomas can not be clearly and easily differentiated by cytology sampling. Surgical analysis remains the gold-standard for discriminating among follicular nodular pathologies of the thyroid. Accordingly other follicular malignancies from the huge follicular adenomas may have been present which would cause obvious changes in the statistical analyses and significantly alter the study's for sensitivity, specificity, PPV and accuracy.⁴

As reported in previous publications, the incidence of malignancy is significantly higher in patients with single nodular calcification than in those with multiple calcifications, suggesting that single nodular calcifications are more closely associated with malignancy than multiple nodular calcifications. Unfortunately, however, the study by Park, et al. did not report data on solitary or multiple calcifications. Another important point, worth considering is the differences in the patients nodules in regards to age and gender, as the incidences of micro and macrocalcifications have been shown to be significantly correlated with patients age (higher number of microcalcifications in patients ≤ 45 years old, compared to older patients, and a lower number of

macrocalcifications in patients ≤ 45 years old compared to older patients).^{5,6}

In conclusion, based on our experience, the major sonographic characteristics of nodules that can be used to predict malignancy consist of the presence of a taller-than-wide or irregular shape, irregular margin with interruption of macrocalcification and nodules that require further evaluation by FNAB.^{1,3,5-7} As well, type and category of macrocalcifications might be more important in the diagnosis of malignancy of nodules than the size of macrocalcifications in the nodule, such as coarse and peripheral egg-shell calcifications being benign with a few exceptions.^{5,7,8}

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