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Histogram analysis of greyscale sonograms to differentiate between the subtypes of follicular variant of papillary thyroid cancer

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AIM: To evaluate the diagnostic value of histogram analysis using ultrasound (US) to differentiate between the subtypes of follicular variant of papillary thyroid carcinoma (FVPTC).

MATERIALS AND METHODS: The present study included 151 patients with surgically confirmed FVPTC diagnosed between January 2014 and May 2016. Their preoperative US features were reviewed retrospectively. Histogram parameters (mean, maximum, minimum, range, root mean square, skewness, kurtosis, energy, entropy, and correlation) were obtained for each nodule.

RESULTS: The 152 nodules in 151 patients comprised 48 non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTPs; 31.6%), 60 invasive encapsulated FVPTCs (EFVPTCs; 39.5%), and 44 infiltrative FVPTCs (28.9%). The US features differed significantly between the subtypes of FVPTC. Discrimination was achieved between NIFTPs and infiltrative FVPTC, and between invasive EFVPTC and infiltrative FVPTC using histogram parameters; however, the parameters were not significantly different between NIFTP and invasive EFVPTC.

CONCLUSION: It is feasible to use greyscale histogram analysis to differentiate between NIFTP and infiltrative FVPTC, but not between NIFTP and invasive EFVPTC. Histograms can be used as a supplementary tool to differentiate the subtypes of FVPTC.

Introduction

Follicular variant of papillary thyroid cancer (FVPTC) is the most common variant of PTC, constituting one-third of all cases.[1,2] It is composed almost entirely of follicles lined

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by cells with the nuclear features of PTC, such as ground-glass nuclei, nuclear grooves, and overlapping nuclei.[3] In recent years, with the increased incidence of thyroid cancer worldwide, FVPTC has been increasingly diagnosed, and it is known to have indolent behaviour.[4–6]

FVPTC can be divided into two subtypes: infiltrative and encapsulated. Encapsulated FVPTC (EFVPTC) can have capsular and/or vascular invasion. Non-invasive EFVPTC is characterized by an encapsulated tumour without invasion, and is associated with a low risk of metastasis and recurrence, so total thyroidectomy and radioactive iodine (RAI) therapy may be deemed overtreatment.[7,8] For this reason, the term "non-invasive follicular thyroid neoplasm with papillary-like nuclear features" (NIFTP) has recently been proposed to replace the phrase "non-invasive EFVPTC.[8] As it has been proposed that distinction between NIFTP and the other FVPTC subtypes reduces the incidence of over-treatment, differential diagnosis of the subtypes of FVPTC has become important.

Greyscale ultrasound (US) is an easily applicable and standard imaging modality used to evaluate thyroid nodules worldwide. Moreover, US criteria for benign and malignant nodules, according to their morphological features, have been suggested and have a high performance level.[9,10] In a recently published report, most NIFTPs lacked malignant US features[11]; however, the report provided no information about differentiation among the FVPTC subtypes; it simply divided the subjects into NIFTP and non-NIFTP groups.

Furthermore, US is highly dependent on the attending radiologist's experience, and it has significant interobserver variations.[12–15] To overcome the limitations of interobserver variations in the evaluation of US, quantitative texture analysis using histogram has been employed in previous reports.[16–19] Such analysis can be used to quantify the spatial variation of grey levels within a region of interest (ROI); such variation is not discernible to the human eye. This objectivity and quantitative nature are the strengths of histogram analysis. Thus, the approach may provide a high degree of diagnostic value with regard to differentiating the subtypes of FVPTC.

Therefore, the purpose of the present study was to evaluate the feasibility of greyscale US and histogram analysis in differentiating the subtypes of the FVPTC.

Materials and methods

Patient selection

The Institutional Review Board approved this retrospective study. Written informed consent was obtained from all patients before US-guided fine-needle aspiration (FNA) or surgery; however, the requirement for informed consent was waived for this retrospective study.

In the present study, 169 nodules of 168 patients with surgically confirmed as FVPTC, who had been diagnosed in a single institution between January 2014 and May 2016, were identified retrospectively. The exclusion criteria were as follows: (1) nodule diameter of ≤5 mm (n=12) in small nodules, the ROI method has lower accuracy,[20] and current guidelines do not recommend FNA in nodules with a diameter of ≤5 mm[9,10]; (2) lack of precise correlation between histopathology and US findings in patients with multiple nodules (n=5). All patients underwent preoperative US within 1 month before surgery. US-guided FNA or core needle biopsy was performed in all patients.[21–23] Ultimately, 152 nodules of 151 patients were included in the present study.

Imaging methods and data collection

B-mode US was performed using an iU22 system (Vision 2010; Philips, Seattle, WA, USA) with a commercially available 7–12-MHz linear-array transducer. All scans were performed by one of seven radiologists with between 2 and 12 years of experience in performing and interpreting thyroid US. Longitudinal and transverse images were obtained for each nodule and some nodules also underwent colour Doppler US.

The US images were reviewed independently by one radiologist and one radiology senior resident with <1 year of experience in thyroid imaging. According to the Korean Thyroid Imaging Reporting And Data System (K-TIRADS), the sonographic features of the thyroid nodules were evaluated in terms of the following factors[10]: size, internal content (solid, predominantly solid or cystic, cystic), echogenicity (marked hypoechogenicity, mild hypoechogenicity, isoechogenicity, or hyperechogenicity), margin (ill-defined, speculate/microlobulate, smooth), orientation (non-parallel or parallel), shape (irregular or round-to-ovoid), calcifications (none, microcalcification, macrocalcification, or rim calcification), halo (present or absent), vascularity on colour Doppler image (none, perinodular vascularity, mild intranodular vascularity (vascularity <50%) or marked intranodular vascularity (vascularity >50%)). Categories of 1–5 were assigned as follows: category 1, no nodule; category 2, benign nodule (spongiform, pure cyst, or partially cystic nodule with comet tail artefact); category 3, low suspicion nodule (partially cystic or isohyperechoic nodule without any of the three suspicious US features); category 4, intermediate suspicion nodule (solid hypoechoic nodule without any of the three suspicious US features or partially cystic or isohyperechoic nodule with any of the three suspicious US features); and category 5, high suspicion nodule (solid hypoechoic nodule with any of the three suspicious US). Suspicious features include microcalcification, non-parallel orientation, and spiculate/microlobulate margin. When the two readers differed over their interpretation of the US features, they reached a consensus by reviewing the images again. The patients' clinical data (age, sex, and histopathological findings) were collected from the database. All histopathology slides for the subtypes of FVPTC were reviewed by an experienced cytopathologist.

The most representative image of the nodule on the longitudinal or transverse scans, i.e., the most clearly visible image of the nodule with no artefacts, was chosen for the analysis. One radiologist drew the ROIs along the border of

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