Ultrasound in Med. & Biol., Vol. 42, No. 10, pp. 2391–2400, 2016

0301-5629/$ - see front matter

http://dx.doi.org/10.1016/j.ultrasmedbio.2016.06.014

● *Original Contribution*

FEASIBILITY STUDY OF ULTRASONOGRAPHIC CRITERIA FOR MICROSCOPIC AND MACROSCOPIC EXTRA-THYROIDAL EXTENSION BASED ON THYROID CAPSULAR CONTINUITY AND TUMOR CONTOUR IN PATIENTS WITH PAPILLARY THYROID CARCINOMAS

Jee Hyun Rim,* Semin Chong,* Han Suk Ryu,† Bo Mi Chung,* and Hye Shin Ahn*

*Department of Radiology, Chung-Ang University Hospital, Chung-Ang University College of Medicine, Seoul, Korea; and
†Department of Pathology, Seoul National University Hospital, Seoul, Korea

(*Received* 29 *April* 2015; *revised* 24 *May* 2016; *in final form* 6 *June* 2016)

Abstract—Our purpose was to evaluate the feasibility of using ultrasonographic criteria of thyroid capsular continuity and tumor contour to differentiate macroscopic extra-thyroidal extension (ETE) from microscopic ETE, as well as non-ETE from ETE. On ultrasonography, we evaluated thyroid capsular continuity (C0 = continuous, C1 = discontinuous, C2 = invisible), and thyroid tumor contour (P0 = in normal parenchyma, P1 = abutting, P2 = bulging), which were grouped into type 1–9 classifications. Either C1–2 or P1–2 was more prevalent in ETE than non-ETE. C1 and P2 tended to be associated with macroscopic ETE, whereas C0 and P1 were significantly associated with microscopic ETE. Types 6, 8 and 9 were more likely to have ETE than non-ETE; type 6 (C1 P2) and type 9 (C2 P2) were significantly associated with macroscopic ETE, whereas type 8 (C2 P1) was associated more with microscopic ETE. Macroscopic and microscopic ETE, as well as non-ETE and ETE, can be differentiated using these pre-operative ultrasonographic criteria. (E-mail: smchong@cau.ac.kr) © 2016 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Ultrasonography, Thyroid gland, Capsules, Thyroid cancer, Papillary.**

INTRODUCTION

Papillary thyroid carcinoma (PTC) is the most common histologic type of differentiated thyroid cancer and accounts for 80% of all thyroid cancers (Park et al. 2009). The most commonly used staging classifications are AGES (patient age, histologic grade of tumor, tumor extent [extra-thyroidal invasion or distant metastases], size of primary tumor); AMES (patient age, presence of distant metastases, extent and size of primary tumor); MACIS (metastasis, patient age, completeness of resection, local invasion, tumor size); and age-related TNM, in which differentiated thyroid cancers can be further divided into low-risk and high-risk groups (Dean and Hay 2000; Gemsenjager et al. 2001; Hu et al. 2007; Moon et al. 2011). In the AGES and AMES classifications, the high-risk groups have higher cause-specific mortality at 20 y than the low-risk groups (39%–39.5% and 1.1%–1.2%, respectively) (Dean and Hay 2000).

The AGES, AMES and MACIS classifications share several prognostic factors, such as patient age, tumor size, extra-thyroidal extension (ETE) of the tumor and metastasis, whereas tumor histologic grade is included only in AGES, and completeness of primary tumor resection is used only in MACIS (Dean and Hay 2000; Gemsenjager et al. 2001). ETE, the definition of which includes (i) extension of the primary thyroid cancer outside the thyroid capsule and (ii) involvement of perithyroidal soft tissues and structures, has been one of the most important and common prognostic factors used in these classification systems (Hu et al. 2007; Ghossein 2009).

Extra-thyroidal extension can be divided into macroscopic ETE and microscopic ETE; the former involves gross tumor invasion, is identified during surgery and is confirmed by histopathologic review; the latter involves tumor invasion beyond the thyroid capsule and is identified during pathologic examination (Arora et al.

Address correspondence to: Semin Chong, Department of Radiology, Chung-Ang University Hospital, Chung-Ang University College of Medicine, 224-1, Heukseok-dong, Dongjak-gu, Seoul 156-755, Korea. E-mail: smchong@cau.ac.kr

2008). According to several previous studies, patients with macroscopic ETE have a significantly higher recurrence rate and lower disease-specific survival compared with patients with microscopic ETE (Gemsenjager et al. 2001; Hu et al. 2007; Arora et al. 2008). To our knowledge, however, there has been no comparative study of ultrasonographic (US) features between macroscopic and microscopic ETE in patients with PTC. Therefore, in this study we propose a set of US criteria for ETE, composed of categories of thyroid capsular continuity and tumor contour, and we compared these criteria between macroscopic and microscopic ETE, as well as between non-ETE and ETE, for pre-operative assessment of ETE in PTC.

METHODS

Our institutional review board approved this retrospective study. Patient informed consent for inclusion into this study was waived.

We searched the operation database of our institution's electronic medical records system for 401 patients who had undergone either total thyroidectomy or thyroid lobectomy for PTC between June 2010 and September 2011. Of these, 191 patients had pathologically confirmed ETE. However, 56 patients with indeterminate ETE, whose pathologic results could not be classified as either microscopic ETE or macroscopic ETE, and 4 patients who did not attend their pre-operative US examination at our institution, were excluded from this study. Absence of ETE was pathologically confirmed in the remaining 210 patients. Fifteen of the 210 patients were excluded from this study because of discrepancy between the US findings and the pathologic reports. Finally, 326 patients with PTC were included in this study, which consisted of 131 patients with ETE (22 men, 109 women; age range, 18–84 y; mean age, 49.4 y) and 195 patients without ETE (34 men, 161 women; age range, 20–78 y; mean age, 47.0 y). Most of the patients underwent a total thyroidectomy (n = 302), and the remaining patients, thyroid lobectomy (n = 24). All patients with ETE were divided into two groups according to their pathology-determined ETE type, based on findings by Arora et al. (2008). Macroscopic ETE was defined as gross tumor invasion identified during surgery and confirmed by histopathologic review. Microscopic ETE was defined as tumor invasion beyond the thyroid capsule and identified at the time of pathologic examination.

Pre-operative US examination was performed with a 5- to 12-MHz linear transducer (IU22, Philips Healthcare, Amsterdam, Netherlands) by a thyroid radiologist with 5 y of experience. Each patient's pre-operative US features were retrospectively reviewed by consensus between a thyroid radiologist with 4 y of experience and a senior resident. Thyroid capsular continuity over the tumor mass (capsular continuity) and the mass contour against the thyroid capsule (tumor contour) were evaluated according as follows: Thyroid capsular continuity was categorized as C0 (continuous echogenic thyroid capsule over tumor mass), C1 (discontinuous hyper-echoic thyroid capsule over tumor mass) or C2 (invisible hyper-echoic thyroid capsule over tumor mass); thyroid tumor contour was categorized into P0 (tumor mass separate from thyroid capsule or tumor mass embedded in normal thyroid parenchyma), P1 (tumor mass abutting thyroid capsule) or P2 (tumor mass bulging from normal thyroid tissue compared with opposite lobe without a mass).

Thyroid capsular continuity and tumor contour were then organized into nine US classifications (Fig. 1): type 1, C0 P0 (separate from a continuous thyroid capsule); type 2, C0 P1 (abutting a continuous thyroid capsule); type 3, C0 P2 (bulging from a continuous thyroid capsule); type 4, C1 P0 (separate from a discontinuous thyroid capsule); type 5, C1 P1 (abutting a discontinuous thyroid capsule); type 6, C1 P2 (bulging from a discontinuous thyroid capsule); type 7, C2 P0 (separate from an invisible thyroid capsule); type 8, C2 P1 (abutting an invisible thyroid capsule); and type 9, C2 P2 (bulging from an invisible thyroid capsule). The longest diameter of the tumor was measured to evaluate the relationship between tumor size and ETE, and the time interval between pre-operative US examination and operation was calculated.

To validate the consensus-based US features and evaluate inter- and intra-observer variability for the US criteria, another two observers—a thyroid radiologist with 4 y of experience (observer 1) and a senior resident (observer 2)—independently analyzed and recorded the US features in all 326 patients according to the US categories and classifications for thyroid capsular continuity and tumor contour. The temporally separate observation of the same observer was repeated in a blinded fashion after 15 d.

Continuous variables were expressed as the mean ± standard deviation, and categorical variables were expressed as the number and percentage. Statistical analyses were performed using PASW Statistics for Windows, Version 18.0 (SPSS, Chicago, IL, USA), and MedCalc for Windows, Version 12.6 (MedCalc Software, Ostend, Belgium). Comparison of the US categories and classifications among three ETE groups (non-ETE group, microscopic ETE group and macroscopic ETE group) were conducted using either the χ^2 test or Fisher's exact test. US categories and classifications that were significantly associated with the three ETE groups were fit into a logistic regression model to obtain odds ratios, 95% confidence intervals and *p* values. The difference