



Sonographic features of papillary thyroid microcarcinoma predicting high-volume central neck lymph node metastasis



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ABSTRACT

Objective: To study the correlations between the sonographic features of papillary thyroid microcarcinoma (PTMC) and the presence of high-volume lymph node metastasis.

Method: Medical records of 2363 PTMC patients were reviewed from October 2013 to December 2015. All the patients with lymph node metastasis identified by histopathology were included. Preoperative sonographic features, such as multifocality, tumour size, echogenicity, calcification, vascularity of papillary microcarcinoma, and capsule invasion, were recorded. Univariate and multivariate analyses were performed to investigate the relationships between sonographic features and high-volume lymph node metastasis (number of metastatic lymph nodes >5).

Results: In total, 152 patients had high-volume central lymph node metastasis (6.4%, 152/2363). Multiple logistic regression analysis showed that the preoperative ultrasonic features of microcalcifications (OR = 3.33, $p = 0.022$), larger tumour size (>7 mm) (OR = 2.802, $p < 0.001$), and capsule invasion (OR = 2.141, $p = 0.006$) were independent risk factors for high-volume lymph node metastasis in the central compartment of PTMC.

Conclusion: The sonographic features of primary papillary microcarcinoma of the thyroid are correlated with high-volume central lymph node metastasis.

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1. Introduction

Papillary thyroid microcarcinoma (PTMC), which is defined as papillary thyroid carcinoma (PTC) with a diameter ≤ 1 cm, is a recent hot research topic due to its increasing annual incidence. A high number of metastatic neck lymph nodes (>5) has been associated with the recurrence of PTC [1,2]. Meanwhile, high-volume neck lymph node metastasis (LNM) was classified as an important risk factor in the 2015 revised American Thyroid Association (ATA) risk stratification system [3]. Ultrasound (US) has a high value in lateral neck lymph node metastasis, with an accuracy of over 90%. However, the exploration of central neck lymph nodes is

unsatisfying, with an accuracy below 50%, because it is affected by gas, bone, and glands [4]. The purpose of this study was to evaluate the ultrasonic features of primary tumours to identify the predictive factors of high-volume central neck lymph node metastasis (CLNM) (>5) and to provide reference information for the clinical treatment of PTMC.

2. Patients and methods

2.1. Patients

A retrospective review was performed on 2363 patients with PTMC, which was confirmed by postoperative pathology between October 2013 and November 2015 in the Peking Union Medical College Hospital. All the patients underwent preoperative ultrasonic examinations to evaluate the features of the tumour and the presence of CLNM. The distribution and number of CLNMs were confirmed by postoperative pathology. According to the 2012

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Chinese management guidelines for patients with thyroid nodules and differentiated thyroid cancer with retention of a recurrent laryngeal nerve and parathyroid, prophylactic central-compartment neck dissection on the ipsilateral side of a lesion is necessary for patients with highly suspected PTC by preoperative US or as determined by ultrasound-guided fine needle aspiration biopsy (US-FNAB). Our study did not include PTMCs that were found in postoperative pathological sections for other reasons and PTMCs that lacked prophylactic central-compartment neck dissection on the ipsilateral side of the lesion.

2.2. Machines and methods

US examinations were performed with Philips IU22/GE Logiq9 sonographic scanners equipped with high-frequency, 5–12-MHz linear probes. Grey-scale and colour Doppler examination were set to the proper conditions for the thyroid gland. The patients were typically examined in the supine position with the neck extended. US features were recorded, including lesion number, lesion size, echogenicity, calcification, envelope, and vascularity of papillary microcarcinoma.

2.3. Sonographic analysis and pathology

US inspection was performed by diagnostic medical sonographers with over 5 years of experience. Similar to the procedure outlined in a previous report [5], US findings were further categorized according to the following features: multifocality (yes or no), tumour size (>7 mm or ≤ 7 mm), echogenicity (hypoechoic or non-hypoechoic), calcification (microcalcifications, macrocalcifications or mixed calcifications), capsular invasion (yes or no), and vascularity (rich blood flow, little blood flow, or no flow). The tumour size was defined as the maximum tumour diameter and was determined digitally by US images. Hypo-echogenicity was defined as decreased echogenicity compared with that of thyroid tissue. Microcalcifications were defined as having a diameter <1 mm [6]. Calcifications were considered macrocalcifications if they became large enough to result in posterior acoustic shadowing. Mixed calcifications consisted of both microcalcifications and macrocalcifications. Loss of the echogenic capsule was assessed as capsular invasion if the normally echogenic rim of the thyroid gland was not sonographically detectable and was presumed to be obscured by the thyroid nodule. Metastatic lymph nodes included the following US features: increased size, rounded shape, absence of a visible hilum, irregular shape, unsharp borders, cystic change, calcifications, and nonhilar vasculature.

Histopathologic analyses of PTMC and mass lymph node metastasis were reviewed by pathologists with more than 10 years of experience. Microscopic observation characterized PTC by true papilla formation, characteristic nuclear changes, and psammoma body formation. According to the 2004 WHO guidelines, the fascicle required only distinctive nuclear features for the diagnosis of PTC [7]. High-volume lymph node metastasis was defined as ≥ 5 metastatic lymph nodes.

The ultrasonography and pathological manifestation of PTMC with CLNM are presented in Fig. 1.

2.4. Statistical analysis

SPSS 23.0 was used for data analysis. The patients were divided into two groups according to the number of metastatic central neck lymph nodes, including high-volume central lymph node metastasis (>5) or non-high-volume central lymph node metastasis (≤ 5). Univariate analysis with the χ^2 -test was performed to analyse the statistical correlations among various factors (gender, age,

multifocality, tumour size, echogenicity, vascularity, calcification, and capsular invasion) and high-volume CLNM. Multivariate logistic regression analysis was used to determine the multivariate correlation of high-volume CLNM. The results are presented as the odds ratios (OR) with 95% confidence interval (CI) and P value. $P < 0.05$ was accepted as statistically significant.

3. Results

3.1. Patient population

In total, 2363 patients with PTMC confirmed by postoperative pathology were included in this study. The distribution and number of their CLNMs were confirmed by postoperative pathology. Among all the patients, 152 (6.4%, 152/2363) had high-volume CLNM. Overall, 569 patients (24.1%, 569/2363) were male, 1794 patients were female (75.9%, 1794/2363), the mean age was 44.0 ± 10.4 years, and the average tumour size was 0.6 ± 0.2 cm.

3.2. Ultrasonic results of CLNM

The sensitivity, specificity, positive predictive value, and negative predictive value of US in evaluating CLNM were 12.5%, 95.2%, 63.6%, and 61.7%, respectively.

3.3. Univariate analysis

The relationships between predictive factors and high-volume CLNM are presented in Table 1. Male gender ($p < 0.001$); young age (<45 years, $p < 0.001$); and the US features of microcalcifications ($p < 0.001$), tumour size (>7 mm, $p < 0.001$), and capsular invasion ($p = 0.003$) were correlated with high-volume CLNM. The number and vascularity of primary lesions were not correlated with the presence of high-volume CLNM.

3.4. Multivariate analysis

Multivariate analysis was performed to determine whether these parameters were independently correlated with high-volume CLNM (Table 2). Male gender (OR = 2.336, $p < 0.001$); young age (<45 years old) (OR = 3.050, $p < 0.001$); and the US features of microcalcifications (OR = 3.331, $p = 0.022$), tumour size (>7 mm) (OR = 2.802, $p < 0.001$), and capsular invasion (OR = 2.141, $p = 0.006$) remained independently predictive of the presence of high-volume CLNM.

4. Discussion

Although the prognosis of PTMC is not poor, lymph nodes are involved in 80% of recurrences [8]. High-volume LNM is an important risk factor in the 2015 revised American Thyroid Association (ATA) risk stratification system. Ultrasonic evaluation of the risk of high-volume CLNM has not been reported. Despite the good overall prognosis of PTC, CLNM after initial surgery remains an important risk factor for local recurrence and is rarely detected clinically [9]. The indications for performing a prophylactic central neck lymph node excision are still debated [10]. Some authors have proposed that if any risk factors for locoregional recurrence are perceived by preoperative or intraoperative assessment, a systematic compartment-oriented lymphadenectomy should be considered because of the high possibility of regional recurrence [11]. Others have suggested that this procedure increases the risk of injury to the parathyroid glands and recurrent laryngeal nerves without any demonstrable benefits in terms of long-term survival [12]. It remains difficult to find patients who are at high risk of

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