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● *Original Contribution*

DIAGNOSTIC EFFICACY OF ULTRASONOGRAPHIC CHARACTERISTICS OF THYROID CARCINOMA IN PREDICTING CERVICAL LYMPH NODE METASTASIS

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Abstract—The goals of this study were to determine the ultrasonographic characteristics of thyroid carcinoma (TC) and to explore the diagnostic efficacy of these ultrasonographic characteristics in predicting cervical lymph node metastasis (LNM). From June 2012 to June 2014, a total of 186 TC patients were recruited from the Central Hospital of Chengde City, Hebei, China. We divided them into two groups: the metastatic group comprised 129 nodules (n = 86), and the non-metastatic group 117 nodules (n = 100). Univariate and multivariate analyses were used to evaluate the relationship between ultrasonographic characteristics and cervical LNM. Spectral Doppler ultrasound was employed to estimate peak systolic velocity, pulsatility index and resistive index. Receiver operating characteristic curves were drawn to evaluate the efficacy of ultrasonographic characteristics in predicting cervical LNM. The sensitivity, specificity, positive predictive value and negative predictive value of ultrasonographic diagnosis were 81.40% (105/129), 92.32% (108/117), 92.11% (105/114) and 81.82% (108/132), respectively. Cervical LNM in TC frequently occurred at the cervical level VI (37.98%) and was located mainly in the middle pole (46.51%) or lower pole (41.09%). Peak systolic velocity and resistive index values were significantly higher in the metastatic group than in the non-metastatic group (both $p < 0.001$). Multivariate analysis revealed that nodular diameter, capsular invasion, microcalcification and flow grade were risk factors for TC patients with cervical LNMs (all $p < 0.05$). Furthermore, receiver operating characteristic curve analysis revealed that nodular diameter, capsular invasion, microcalcification and flow grade had excellent accuracy in predicting cervical LNM. We conclude that ultrasonographic characteristics of TC, including maximum nodular diameter, capsular invasion, microcalcification and flow grade, may predict cervical LNM. (E-mail: wanghongwh0325@163.com) © **2016 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Papillary thyroid carcinoma, Ultrasound, Cervical lymph node, Lymph node metastasis.**

INTRODUCTION

Thyroid carcinoma (TC), the most common endocrine malignancy, currently constitutes 1% to 1.5% of all malignant cancers in humans (Lukas et al. 2013). In the last three decades, the incidence of TC has been steadily rising worldwide. Approximately 1.0%–1.5% of new patients are diagnosed with TC annually in the United Sates, and the incidence is increasing in Australia, Canada and Western Europe (Kahn et al. 2012; Pellegriti et al. 2013). TC comprises differentiated TC, which includes papillary thyroid carcinoma (PTC), follicular TC, medullary TC and anaplastic TC (Kapiteijn et al. 2012). Among these different types, PTC is the cancer with the greatest incidence, approximately 85%, with minimal mortality and low recurrence rate (Carling et al. 2012; Lee et al. 2011). Although most TC patients have better overall survival compared with patients with other cancers, it is significant that lymph node metastasis is common, especially cervical metastases; a 15% rate of recurrence for the 10-y period after surgery has been reported, even for TNM stage I cancers (Kim et al. 2012). The management of TC has changed and improved substantially in the past several decades, largely as a result of the availability of advanced diagnostic tools and the rapid increase in comprehension of the genetic pathogenesis of TC with a large amount of epidemiologic data (De Groot and Mestman 2012; Sipos and Mazzaferri

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2010). Additionally, as for the progression and development of treatment of TC, the identification of TC and an aggressive phenotype may, in conjunction with surgery optimization, adjuvant therapy and long-term follow-up, help guide management of patients with TC (Hughes et al. 2010; Yip et al. 2011).

Cervical lymph node metastasis (LNM) in TC is very common, with the incidence rate ranging from 30% to 80%, and metastatic lymph nodes cab cause cervical lymphadenopathy because of the abnormal size, number and consistency of nodes (King et al. 2014; Takada et al. 2011). It has been reported that cervical lymph node status is associated with the extent and number of nodes in ipsilateral, contralateral or bilateral compartments and with disease conditions including size of metastasis and extracapsular spread, which may even have a great effect on prognosis (Smith et al. 2012). To determine the therapeutic direction, the knowledge of cervical lymph node status is required. Patients with clinically positive cervical LNMs were treated with the standard procedure of modified radical neck dissection, but patients with clinically negative cervical LNMs were only carefully managed with selective treatment such as elective neck resection or a "watchful waiting policy" (Liao et al. 2012). However, the main challenge was considered to be the diagnostic accuracy of cervical LNM in TC.

There is evidence that in improving the accuracy of diagnosing cervical centrally and laterally, different imaging modalities may have advantages; for example, magnetic resonance imaging, positron emission tomography, computed tomography and ultrasonography (US) all, to some extent, may help discriminate malignant from benign TC on the basis of lymph node status in the neck (Choi et al. 2010). It has been reported that US may be the optimal imaging modality, with great sensitivity and specificity for the detection of metastatic lymph nodes, and has been used to obtain several vital ultrasonographic characteristics like shape, echogenicity and echogenic hilum, calcifications, vascularization characteristics, nodal border and intranodal cystic necrosis (Rosario et al. 2005). Furthermore, the use of US is considered a favorable option for the evaluation of cervical LNMs in patients with TC; such ultrasonographic characteristics as micro- or macrocalcification, cystic changes, shape (long/transverse diameter), vascular pattern and focal or diffuse hyperechogenicity serve in the diagnosis of metastatic lymph nodes in the neck (Kim et al. 2008; Leboulleux et al. 2007). In this study, we explored the diagnostic efficacy of ultrasonographic characteristics of TC in predicting cervical LNMs, which may also help to more accurately determine the pre-operative status of cervical LNMs.

METHODS

Ethics statement

This study was conducted with the approval of the institutional ethics committee of the Central Hospital of Chengde City, Hebei, China. All participants willingly provided written informed consent. The experimental principles were in accordance with the Declaration of Helsinki (Salako 2006).

Patients

From June 2012 to June 2014, a total of 186 TC patients (37 males, 149 females; median age: 49.53 y, range: 20–79 y), including 177 with PTC, three with follicular TC and six with medullary TC, were recruited from the Central Hospital of Chengde City. The diagnosis of TC was confirmed by fine-needle aspiration biopsy (Amedee and Dhurandhar 2001). The Exclusion criteria for patients were (i) incomplete clinical data, resulting in failed statistical analysis; (ii) presence of other malignancies; and (iii) pre-operative endocrine therapy, radiotherapy, chemotherapy or other oncotherapy. All participants underwent thyroidectomy or puncture after an examination recording the ultrasonographic characteristics of the lymph nodes. Postoperative pathologic results revealed 246 TC nodules in all patients; 86 patients (129 nodules) had cervical LNMs (metastatic group) and 100 patients (117 nodules) had no LNMs (non-metastatic group).

Ultrasonography

A Philips ATL 5000 (Philips Ultrasound, Bothell, WA, USA) unit was used with a 7.5- to 12.0-MHz linear probe (GELogiq9) for ultrasonography. The anterior compartment of all participants in the supine position was fully exposed to ultrasound throughout the examination. All suspicious nodules were detected to obtain images in the declinate, transverse and longitudinal orientations. We recorded the ultrasonographic characteristics of the thyroid gland, including size, margin, location, aspect ratio, internal architecture, echogenicity, nodular diameter, calcification, degree of vascularization and extent of contact between the border and capsule. Images of cervical lymph nodes were also obtained, revealing several features like shape, size and echogenicity for marking cervical compartments with metastatic lymph nodes. Spectral Doppler ultrasound was employed to estimate peak systolic velocity (PSV), pulsatility index and resistive index (RI).

Ultrasound criteria and imaging analysis

Ultrasound criteria for the percentage of contact between the perimeter of the nodule and the thyroid capsule were as follows: (i) 0% contact = no thyroid tissue intervening between the primary tumor and the capsule;

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