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● *Original Contribution*

DIAGNOSTIC ACCURACY OF COMPUTER-AIDED ASSESSMENT OF INTRANODAL VASCULARITY IN DISTINGUISHING DIFFERENT CAUSES OF CERVICAL LYMPHADENOPATHY

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Abstract—Ultrasound is useful in assessing cervical lymphadenopathy. Advancement of computer science technology allows accurate and reliable assessment of medical images. The aim of the study described here was to evaluate the diagnostic accuracy of computer-aided assessment of the intranodal vascularity index (VI) in differentiating the various common causes of cervical lymphadenopathy. Power Doppler sonograms of 347 patients (155 with metastasis, 23 with lymphoma, 44 with tuberculous lymphadenitis, 125 reactive) with palpable cervical lymph nodes were reviewed. Ultrasound images of cervical nodes were evaluated, and the intranodal VI was quantified using a customized computer program. The diagnostic accuracy of using the intranodal VI to distinguish different disease groups was evaluated and compared. Metastatic and lymphomatous lymph nodes tend to be more vascular than tuberculous and reactive lymph nodes. The intranodal VI had the highest diagnostic accuracy in distinguishing metastatic and tuberculous nodes with a sensitivity of 80%, specificity of 73%, positive predictive value of 91%, negative predictive value of 51% and overall accuracy of 68% when a cutoff VI of 22% was used. Computer-aided assessment provides an objective and quantitative way to evaluate intranodal vascularity. The intranodal VI is a useful parameter in distinguishing certain causes of cervical lymphadenopathy and is particularly useful in differentiating metastatic and tuberculous lymph nodes. However, it has limited value in distinguishing lymphomatous nodes from metastatic and reactive nodes. (E-mail: aniltahuja@cuhk.edu.hk) © 2016 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Lymph nodes, Ultrasonography, Blood vessels, Image processing, Computer assisted, Power Doppler, Vascularity index.**

INTRODUCTION

Patients with head and neck cancers, lymphoma and tuberculosis often present with palpable neck nodes. Accurate diagnosis of the causes of cervical lymphadenopathy is important because the treatments for these diseases differ. In patients with head and neck cancer, accurate assessment of metastatic cervical lymph nodes is particularly crucial because it helps to evaluate patient prognosis and aids treatment planning. In patients with proven head and neck primary squamous tumor, the presence of a metastatic cervical lymph node on one side of the neck reduces the 5-y survival rate to 50%, and the presence of bilateral metastatic lymph nodes in the neck reduces the survival rate to 25% (Som 1992).

Ultrasound-guided fine-needle aspiration and cytology (FNAC) is a common diagnostic method for patients with cervical lymphadenopathy. The reported diagnostic accuracy of FNAC of cervical lymphadenopathy ranges between 82.2% and 88.7% (Hafez and Tahoun 2011; Rajbhandari et al. 2013). In identifying cervical tuberculous lymph nodes, FNAC has a diagnostic accuracy of 72.3% to 85.4% (Khan et al. 2015; Kim et al. 2013). However, 13.8% of patients undergoing FNAC require repeated aspirations, predominantly because of inadequate aspirates (52.4%) and non-diagnostic descriptive reports (43.7%) (Goyal et al. 2014).

Ultrasound is a useful imaging tool and is more sensitive than neck palpation in the assessment of cervical lymphadenopathy (Haberal et al. 2004; Giacomini et al. 2013). On ultrasound examination of cervical lymph

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nodes, gray-scale ultrasound assesses the nodal morphology, whereas color and power Doppler ultrasound evaluates intranodal vascularity. It has been reported that color and power Doppler ultrasound is useful in assessing lymph node vascularity and helpful in the differential diagnosis of cervical lymphadenopathy (Ahuja and Ying 2003; Giacomini et al. 2013; Park and Kim 2014). Normal and reactive lymph nodes appear predominantly avascular or exhibit hilar vascularity (Ying and Ahuja 2003). Peripheral vascularity with or without hilar vascularity is common in metastatic and lymphomatous nodes, whereas displaced vascularity with apparently avascular areas is frequently found in tuberculous nodes (Ahuja and Ying 2003; Giacomini et al. 2013; Park and Kim 2014). Moreover, tumor angiogenesis and the related proliferation of intranodal vasculature cause metastatic and lymphomatous lymph nodes to have higher vascularity than benign and tuberculous nodes (Wu et al. 1998a). Therefore, the abundance of intranodal vascularity, which can be expressed as the vascularity index (VI), could be a useful imaging parameter to distinguish different causes of cervical lymphadenopathy. This intranodal vascular abundance can be evaluated both qualitatively and quantitatively. In qualitative assessment, the intranodal vascularity is graded on a Likert scale according to the abundance of vascularity and vessels found within the lymph node (Wu et al. 2000; Ying et al. 2000). In quantitative assessment, the vascularity of lymph nodes is quantified using a customized image post-processing program and is expressed as a numerical value (Wu et al. 1998b, 2000). A recent study found that quantitative assessment of intranodal vascularity is more reliable and accurate than qualitative assessment in differentiating reactive and metastatic lymph nodes (Lam et al. 2016).

Despite the aforementioned reports, overall, in the literature there is limited information about the diagnostic accuracy of quantitative assessment of the intranodal VI in distinguishing between the various causes of cervical lymphadenopathy. Therefore, this study was undertaken to evaluate the diagnostic accuracy of the intranodal VI in distinguishing metastatic, lymphomatous, tuberculous and reactive lymph nodes and to determine the optimum cutoff value of intranodal VI in the differential diagnosis. The clinical significance of the study is to provide an additional parameter that is objective and reliable for differential diagnosis of various causes of cervical lymphadenopathy.

METHODS

The study was approved by the Human Subject Ethics Subcommittee of the Department of Health Technology and Informatics, Hong Kong Polytechnic University. We retrospectively reviewed power Doppler sonograms of 347 patients with palpable cervical lymph nodes. Patients were selected consecutively from our patient database, and patients without confirmed cytology or pathology results for the lymph nodes were excluded. All data from the study were obtained from the routine clinical ultrasound examinations, and the ultrasound examinations were performed using a standard of care clinical protocol. Among the 347 patients, 155 had known head and neck cancers or primary tumors in other body regions with proven metastatic cervical nodes (54 nasopharyngeal carcinoma, 30 oral cavity carcinomas, 25 papillary carcinomas of the thyroid, 23 pharyngeal and laryngeal carcinomas, 14 lung carcinomas, 6 breast carcinomas, 1 testicular carcinoma, 1 colon carcinoma, 1 gastric carcinoma); 23 patients had lymphomatous nodes (20 patients with non-Hodgkin's lymphoma and 3 patients with Hodgkin's disease); 44 patients had tuberculous lymph nodes; and 125 patients had reactive nodes (none of these patients had any known carcinoma, and patients underwent clinical follow-ups in the outpatient department and remained well).

The neck ultrasound examination of the 347 patients was performed by the same operator using the same ultrasound scanning protocol, whereas image analysis of the intranodal VI was conducted by another operator. The operator was blinded to the FNAC result of the lymph nodes at the time of image analysis. All ultrasound examinations were performed on a Philips IU22 ultrasound unit using a 5- to 12-MHz linear transducer (Philips, Bothell, WA, USA). In each patient, the cervical nodes were assessed with gray-scale and power Doppler ultrasound, and the lymph node that exhibited the most abundant vascularity was included in the study. Settings for power Doppler ultrasound were standardized for detecting blood vessels with low blood flow velocity: high sensitivity, low wall filter, pulsed repetition frequency (PRF) = 700 Hz and medium persistence. The color gain was standardized and increased at the beginning to show color noise (low amplitude, intermittent and scattered color signals) and then decreased until the noise disappeared (Ying et al. 2000).

On power Doppler ultrasound examination of each lymph node, multiple sonograms at different scan planes were obtained, and the sonogram that revealed the most abundant intranodal vascularity was selected for measurement of the intranodal VI. In assessment of the intranodal VI, the degree of vascularity was evaluated using the software program MATLAB (Version 7.3.0.267 R2006b, The MathWorks, Natick, MA, USA) and a customized algorithm for color signal quantification of Doppler images (Lam et al. 2016; Ying et al. 2009). Power Doppler ultrasound images retrieved from the