Differential diagnosis of malignant cervical lymph nodes at real-time ultrasonographic elastography and Doppler ultrasonography

Kemal Arda, Nazan Ciledag, Pelin Demir Gumusdag

PURPOSE
Real-time ultrasonographic elastography is a new imaging technique which is used in characterizing the difference in hardness between pathological and normal tissue. The purpose of our study was to evaluate the diagnostic performance of real-time ultrasonographic elastography and Doppler ultrasonography (DUS) individually and combined in differentiation of benign and malignant cervical lymph nodes (LN).

PATIENTS AND METHODS
Fifty-one patients (12 men, 39 women) referred for fine-needle aspiration or surgical biopsies of suspected cervical lymph nodes were examined with gray scale ultrasonography, power DUS, and real-time ultrasonographic elastography. During DUS examination vascularity and resistance index (RI) values were evaluated. A five-group elastographic colour code pattern was used to evaluate the ultrasonographic elastograms for LN (pattern 1, an absent or a very small hard area; pattern 2, hard area <45%; pattern 3, hard area ≥45%; pattern 4, peripheral hard and central soft areas; pattern 5, hard area occupying entire solid component with or without soft rim). In addition, strains of LN and surrounding muscles were measured on elastograms, and the muscle-to-LN ratio (strain index) was calculated. Real-time ultrasonographic elastography and DUS results were compared with the final diagnosis obtained by fine-needle aspiration cytology analysis and/or by surgical pathology. The diagnostic potential of the examined criteria for malignancy was evaluated with univariate analysis and multivariate generalized estimating equation regression p<0.05 indicated statistical significance.

RESULTS
A strain index higher than 2.45 and colour pattern 4-5 had high utility in malignant LN classification with 93.8% sensitivity and 89.5% specificity (p<0.001). The results were significantly better than those obtained by using DUS characterization – that is, RI greater than 0.57 – which had 78.9% sensitivity (p<0.001).

CONCLUSION
Real-time ultrasonographic elastography had 93.8% sensitivity and 89.5% specificity in the differentiation of benign and malignant cervical LN in patients referred for fine-needle aspiration or surgical biopsies with suspicion of malignancy. Real-time ultrasonographic elastography and DUS in addition to gray scale ultrasonography may improve the differential diagnosis of LN.

Ultrasonography and DUS are useful imaging techniques in evaluation of localization, number, size, echo characteristics and vascularity of lymph nodes. However, the indication of these methods as benign or malignant LN, have low accuracy, therefore causing difficulties in judgement. Real-time ultrasonographic elastography is new imaging technique, displays tissue elasticity. In colour elastograms, increasing tissue hardness from benign to malignant lesion appears in ascending order as red, yellow, green, and blue. Ultrasonographic elastography is used to examine several organs such as; breast1 2, thyroid3, prostate4, cervix5, and liver6. This technique is promising imaging technique that can be used in the differentiation of benign and metastatic lymph nodes. However, to our knowledge, only limited numbers of studies have been reported on real-time ultrasonographic elastography application on characterization of lymph nodes.

Evaluate the accuracy of real-time ultrasonographic elastography and Doppler ultrasonography in the differentiation of benign and metastatic cervical lymph nodes in patients suspected of head or neck or breast malignancies, with histopathologic nodal findings as the reference standard.

The purpose of the study was to investigate the diagnostic performance of real-time ultrasonographic elastography and DUS individually and combined in differentiation of benign and malignant cervical LN.
PATIENTS AND METHODS

This was a prospective study. The study protocol was approved by the hospital review board; written informed consent was received from all patients for undergoing both DUS and real-time ultrasonographic elastography. From November 2008 to May 2009 51 cervical lymph nodes in 51 patients (12 men, 39 women; age ranged 9-72 mean age, 49.6 years ± 14.8 (standard deviation)) referred for fine-needle aspiration or surgical biopsies of suspected cervical lymph nodes, in which the final diagnosis was not known, were enrolled. All patients were examined with gray scale, power Doppler, and real-time ultrasonographic elastography by using the Hitachi EUB 5500, and a 10 MHz linear probe, by two radiologists. One of the radiologists had 20 years’ and the other had 7 years’ experience with gray scale ultrasonography performed the gray scale, and Doppler ultrasonography, and real-time ultrasonographic elastography. All interpretations performed before biopsy, and the radiologists were blinded to the patients’ final diagnosis. Decisions regarding the findings were reached by consensus.

Gray-scale ultrasonography was performed first for all patients. Power and spectral DUS were performed in second step. Then real-time ultrasonographic elastography was performed by using the same probe.

Regional LN distribution was determined according to the 1997 American Joint Committee on Cancer (AJCC) criteria for LNs, and LNs in level 7, and LNs in level 7 was referred to Cancer (AJCC) criteria 1997 American Joint Committee determined according to the same probe. Power and spectral DUS were performed in second step. Then real-time ultrasonographic elastography was performed by using the Hitachi EUB 5500, and a 10 MHz linear probe, by two radiologists. One of the radiologists had 20 years’ and the other had 7 years’ experience with gray scale ultrasonography performed the gray scale, and Doppler ultrasonography, and real-time ultrasonographic elastography. All interpretations performed before biopsy, and the radiologists were blinded to the patients’ final diagnosis. Decisions regarding the findings were reached by consensus.

Gray-scale ultrasonography was performed first for all patients. Power and spectral DUS were performed in second step. Then real-time ultrasonographic elastography was performed by using the same probe. Regional LN distribution was determined according to the 1997 American Joint Committee on Cancer (AJCC) criteria for LNs, and LNs in level 7 were excluded. At gray-scale US, LNs were identified, and LNs characteristics such as size, short-axis diameter, short-to-long axis diameter ratio, and echogenicity, calcifications, and lymph nodes hilum were evaluated. At power DUS the vascularity and resistance index (RI) values of the LNs were evaluated. For real-time ultrasonographic elastography, repeated compression with light pressure from upward to downward direction followed by decompression was performed until 4 green lights is stabilized on compression scale. Real-time ultrasonographic elastography and gray-scale ultrasonography images simultaneously appeared on the same image divided into two panels. By two radiologists, elastograms were together, subjectively decided five-group colour pattern depending on the distribution of the blue (hard), and soft (red, green) area in LN (pattern 1, an absent or a very small hard area; pattern 2, hard area <45%; pattern 3, hard area ≥45%; pattern 4, peripheral hard and central soft areas; pattern 5, hard area occupying entire solid component with or without soft rim). In addition, strains of LN and surrounding muscles were measured on elastograms, and the muscle-to-LN ratio (strain index) was calculated. All of the patients underwent fine-needle aspiration biopsy or excisional biopsy. The time interval between real-time ultrasonographic elastographic evaluation and biopsy were less than 5 days. Cytological or pathologic diagnosis of LNs were compared with real-time ultrasonographic elastography and DUS features.

Quantitative variables were compared by using the Mann- Whitney U test. Qualitative variables were compared by using the X² test. The elastographic characteristics of each lymph node were registered separately and processed blindly for statistical evaluation. The value of each visual and qualitative criterion that showed the highest diagnostic accuracy in the distinction between benign and metastatic lymph nodes was selected as the cut off value. One-way analysis of variance was performed to assess the differences in elastographic characteristics between the metastatic and benign lymph nodes. A multivariate analysis was performed by using the generalized estimating equation method to select the variables (i.e., examined US and elastographic criteria) that were independently associated with lymph node metastasis. Quantitative data are presented as means ± standard deviation. P ≤ 0.05 indicated statistical significance. The statistical analyses were performed by using SPSS 10.0.

RESULTS

By AJCC levels, 9 nodes were in level 1, 14 in level 2, 18 were in level 3, 8 had in level 4, and 2 in level 5. The prevalence of LN metastases was 62% (32/51). Among the malignant LNs, 14 had primary squamous cell carcinoma, 7 had primary site in breast, 4 had primary thyroid carcinoma, 3 had malignant melanoma metastases primary site in head or neck, two had nodular sclerosing Hodgkin’s lymphoma and two was B cell Hodgkin’s lymphoma. Twenty-one LNs were histopathologically diagnosed as reactive. At gray scale ultrasonography, the cut off short-to-long axis diameter ratio was 0.5; ≤0.5 was reactive and >0.5 was metastatic with 61% sensitivity, and 73% specificity p<0.01). When the RI value of 0.57 was taken as the cut-off point at DUS, the sensitivity and specificity of elastography were 78.9% and 90.6 %. Sensitivity, specificity, positive predictive value and negative predictive value of RI values at Doppler ultrasonography were 78.9%, 90.6%, 83.3% and 87.9%(p<0.001), respectively. During real-time ultrasonographic elastography, stable compression frequency scale 4 was needed to obtain, and only this elastograms enrolled. When the strain index value of 2.45 was taken as the cut-off point, the sensitivity and specificity of elastography were 93.8% and 89.5%. The mean strain index value of benign lymph nodes were 1.4±0.97 (Figure 1), and the mean strain index values of malignant lymph nodes were 4.5±1.0.
10.9±14.9 (Figure 2). The cut off line of elastographic colour pattern for reactive versus malignant LN was set between patterns 1 and 3; patterns 4–5 were considered malignant (Figure 3). Sensitivity, specificity, positive predictive value and negative predictive value of real-time ultrasonographic elastography were 89.5%, 93.8%, 89.5% and 93.8% (p<0.001), respectively, for elastographic colour pattern and strain index values.

DISCUSSION

Ultrasoundography is frequently performed in cervical LNs with suspicion of malignancy. Several studies have been reported on diagnostic criteria of ultrasonography of benign and malignant LNs. Lymph node size, short-axis diameter (in mm), short-to-long-axis diameter ratio, echogenicity, calcifications, lymph nodes hilum and shape have been previously described as the criteria for malignancy detection, but all of them have low sensitivity and specificity.

The assessment of internal nodal vascularity and RI values are additional diagnostic criteria for the diagnosis of malignant LNs with high specificity but low sensitivity.

In our study, gray scale ultrasonography had low sensitivity and specificity. At Doppler US, RI value had high specificity but low sensitivity. These findings correspond to previously published reports that have the value of power Doppler US can not compete with that of fine-needle aspiration biopsy in the diagnosis of malignant LNs.

Our results in differential diagnosis of benign and malignant lymph nodes at real-time ultrasonographic elastography show that the majority of benign lymph nodes had similar colour pattern as the surrounding anatomical structures. In contrast, majority of malignant LNs were partially or substantially blue on elastograms, and this finding may reflect the differences of elasticity properties between malignant LNs and surrounding tissue or a desmoplastic reaction that creates a stiff rim around malignant LNs. In our study, elastography colour pattern and strain index values had high diagnostic accuracy with high specificity.

Our findings suggest that real-time ultrasonographic elastography with its high specificity, may be helpful in selection of cervical LNs, which may improve the differential diagnosis of LN.
REFERENCES