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Evaluating the reliability of ultrasonographic parameters in differentiating benign from malignant superficial lymphadenopathy

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ABSTRACT

Diagnosis of malignant lymphadenopathy is of particular importance for treatment planning, before treatment staging and also for prognosis determination. Currently various diagnostic procedures are used to differentiate benign and malignant lymphadenopathy which are invasive and costly. Ultrasonography as a noninvasive, low-cost and accessible method is proposed. The aim of this study was to evaluate the reliability of some ultrasonographic parameters in differentiating malignant from benign superficial lymphadenopathies. In this study ultrasonography was performed for lymph nodes of 100 patients who were eligible for pathological evaluation of superficial lymphadenopathy. The most accessible lymph nodes were marked and biopsied. Sonographic and pathologic results were compared. The sensitivity and specificity of the test and the appropriate cutoff point was determined based on the Receiver Operating Characteristics (ROC) curve using SPSS Ver.17. From 100 evaluated lymph nodes 55 were benign and 45 were malignant. There was no significant difference between malignant and benign lymph nodes in terms of cortical and medullary thickness (p=0.055),but there was a significant difference between benign and malignant lymph nodes in terms of blood supply pattern and mean of Pulsatility Index (PI) (P=.007) and Resistive Index (RI) (P<0.001) . The cortex thickness of 7.95 mm with 62.2٪ sensitivity, 72.7٪ specificity and 70٪ accuracy was the appropriate cutoff point in differentiating malignant and benign lymphadenopathy. The color Doppler criteria in combination with gray scale ultrasonography could be helpful to select patients for biopsy or Fine Needle Aspiration (FNA), but cannot fully replace pathological evaluation.

Keywords: Ultrasonography, Lymphatic Diseases, Diagnosis

INTRODUCTION

Enlarged lymph nodes may be a part of the clinical signs of a malignant process. Therefore, lymphadenopathy diagnosis is of particular importance [1]. Diagnosis of malignant lymph nodes is important for staging and treatment planning and also for prognosis determination [1-3]. In head and neck malignancies metastasis to neck lymph nodes reduces patient`s survival as 50%. Currently various diagnostic procedures are used to differentiate benign and malignant lymphadenopathy which are invasive and costly including; lymph nodes surgical removal, Magnetic Resistance Imaging (MRI), CT scan (Computed Tomography) and Position Emission tomography (PET) [4]. Invasive procedures such as removal of auxiliary lymph nodes in breast cancer causes patient`s inability, as well as, many patients may not have metastatic lymph nodes and not take advantage of it, therefore using a fast, accessible,

low-cost and non-invasive method with high sensitivity and specificity to identify the involved lymph nodes is necessary [5]. Color Doppler Ultrasonography is proposed as a method to distinguish between benign and malignant lymphadenopathy [2, 6-8]. However, the validity of Doppler indices and also specified amount of vascular patterns in the differentiation between benign and malignant lymphadenopathy has not been determined yet [3].

The aim of this study was to evaluate the reliability of some ultrasonographic parameters in differentiating malignant and benign superficial lymphadenopathies. As well as we evaluated the sensitivity and specificity of cortical thickness as a diagnostic marker for well-differentiated benign lymphadenopathy from malignant lymphadenopathy and determined an appropriate diagnostic cutoff point.

MATERIALS AND METHODS

This cross-sectional study conducted on 100 patients who were eligible for pathological evaluation of superficial lymphadenopathy with FNS method in Afzalipour hospital in Kerman, Iran in 2013. According to similar studies [9] and 96% sensitivity of ultrasonography to diagnosis nodes with cortex thickness less than 1.5mm and 84% sensitivity of ultrasonography to diagnosis nodes with cortex thickness of 1.5-2.5 mm and also considering the type I error of 0.05and type two error of 0.20 and using related formula the sample size was determined as 100 lymph nodes [10]. Inclusion criteria were having palpable superficial lymph nodes which were considered for histological investigation by the physician. Patients who were examined for lymphadenopathy previously and their disease (regardless to malignancy or benignity) was diagnosed with other methods rather than ultrasonogrphy and referred to hospital for further investigation in terms of disease recurrence were exclude from the study.

Firstly, ultrasonography was performed for lymph nodes of 100 patients by a radiologist who was unaware of initial diagnosis. The ultrasonography was performed using Medison Accuvix V10 ultrasound system made by Samsung and level probes of 10MHz. Ultrasonographic parameters including; the cortex thickness, medullary thickness, blood supply pattern also semi-quantitative indicators including; Resistive Index and Pulsatility Index of the most accessible lymph nodes were measured. The lymph nodes were marked by radiologist through ultrasound guidance and FNA was performed or they were removed by a surgeon. Samples were evaluated pathologically then pathological and ultrasonography results were then matched and compared.

Data were analyzed using SPSS Ver.17. Chi-square test, Fisher's exact test and t-test were used to analyze the data. The sensitivity and specificity of the test and the appropriate cutoff point was determined based on the Receiver Operating Characteristics (ROC) curve. The significance level was determined as $p<0.05$.

RESULTS

A total of 100 lymph nodes from 100 patients were examined, regardless of age and sex. The location of the lymph nodes in order of frequency consisted of; cervical 49, auxiliary 22, inguinal 8 and from other parts of the body 21. From 100 evaluated lymph nodes 55 were reactive (benign) and 45 were infiltrative (malignant).

The mean and standard deviation of PI for malignant nodes was 1.35±0.60 and for benign nodes it was 1.05±0.49 .The difference was significant statistically ($p=0.007$). Also the mean and standard deviation of RI for malignant nodes was 0.73±0.19 and for benign nodes was 0.60±0.15 .This difference was also significant statistically ($p<0.001$).

The average and standard deviation of cortex thickness in malignant nodes was 11.37±8.41mm and for benign nodes was 6.58±4.75. The difference was significant statistically ($p=0.001$).

The ratio of cortex thickness to medullary thickness was more than 0.75 in 55 cases in which 35 (63.63%) cases were benign nodes and 20 (36.36%) cases were malignant nodes. Medullary thicknesses in 45 cases were almost zero in which 20(44.44%) cases were benign and 25(55.67%) cases were malignant nodes. Generally there was no significant difference between malignant and benign lymph nodes in terms of cortical and medullary thickness ($p=0.055$). (Table 1)

In terms of blood supply pattern the lymph nodes were divided into four categories including; peripherals, central, mixed (peripherals and central) and avascular. The blood supply pattern in 1 case was avascular and in 7 cases it was

both peripherals and central. In 28 malignant nodes the blood supply pattern was peripheral and in 12 cases was central. In 21 benign cases the blood supply pattern was peripheral and in 31 cases was central. There was a significant difference between benign and malignant lymph nodes in terms of blood supply pattern (p=0.005). (Table 1)

The ROC showed 0.70 that means accuracy of cortex thickness in differentiating benign and malignant superficial lymphadenopathy is 70%.The sensitivity and specificity of cortex thickness in different cutoff points was determined.(Table 2) ,(Figure 1)

The cortex thickness of 7.95 mm with 62.2٪ sensitivity, 72.7٪ specificity and 70٪ accuracy was the appropriate cutoff point in differentiating malignant and benign lymphadenopathy.

Table 1. Frequency distribution of lymph nodes in terms of the ratio of cortex thickness to medullary thickness and the blood supply pattern

		Benign		Malignant		P Value
		No.	%	No.	%	
The ratio of cortex thickness to medullary thickness	<0.75mm	35	63.63	20	44.44	0.055
	medullary thickness=0	20	36.37	25	54.56	
Total		55	100	45	100	
The blood supply pattern	Peripheral	21	40.38	28	70	0.005
	Central	31	59.62	12	30	
Total		52	100	40	100	

Table 2. The cortex thickness sensitivity and specificity

The cortex thickness (mm)	Sensitivity (%)	Specificity (%)
7.15	62.2	69.1
7.6	62.2	70.9
7.95	62.2	72.7
8.1	57.8	74.5
8.3	57.8	76.4

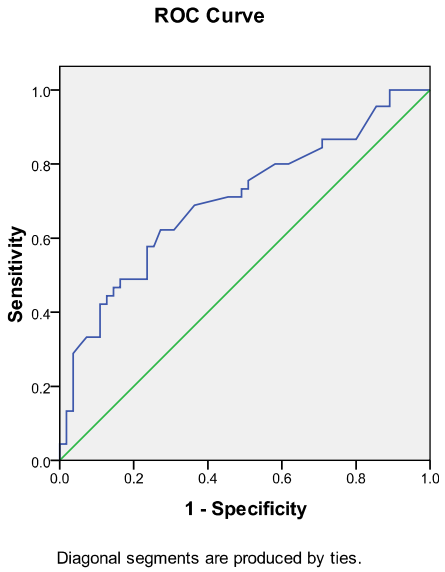

Figure 1. ROC of lymph nodes cortex thickness

DISCUSION

Based on clinical observations it seems that the thickness of the cortex to the medulla in benign and malignant lymphadenopathies changes differently, therefore this ratio was considered as a new ultrasonographic parameter in

this study. Meanwhile the results of the study showed that there was no significance in terms of this ratio in benign and malignant lymphadenopathies. Although the results showed that the cortex thickness in malignant nodes was more than benign nodes. This finding was in consistent with the results of Cho et al. [9].

Given the difference in cortex thickness in lymph nodes this characteristic was considered as differentiating parameter in benign and malignant superficial lymphadenopathies. Also the cortex thickness of 7.95 mm with 62.2% sensitivity, 72.7% specificity and 70% accuracy was determined as appropriate cutoff point in differentiating malignant and benign lymphadenopathies.

Large malignant tumors had angiogenesis factors and stimulate the new blood vessels growth. These blood vessels are thin-walled and often do not have the muscle layer and also have irregular anastomosis and shunts and do not follow the normal blood supply pattern of the lymph nodes. This abnormal blood supply pattern may be seen by color Doppler [8]. Results of present study showed that the dominant pattern of blood supply of malignant nodes were superficial, in other words superficial pattern of blood supply is in the interest of malignant tumors.But it should be considered that the central blood supply pattern does not rule out malignancy. The findings of Na et al. were similar with our result. They evaluated the PI and RI blood supply pattern and compared them with pathological findings. The results showed that in 94% of benign lymph nodes the blood supply pattern was normal while in 98% of malignant lymph nodes the blood supply pattern was abnormal [6].

In a study by Shirakawa et al. in 85.4% of metastatic lymph nodes, 40.5% of lymphomatosis and 7.7% of benign lymph nodes the extrahillar vessels were observed [11]. In a study by Chikui et al the color-flow parameter had the lowest predictive value for cervical lymph node metastasis (2), this study was not in consistent with our study. Perhaps the reason for this difference is the population of the study. Because their study was retrospective and also was limited to those patients with known cervical squamous cell carcinoma, while our patients were not known before the study and metastatic lymphomas were not separated from other total superficial lymph nodes and they were evaluated regardless to the type of disease.

In this study the PI and RI were evaluated .The results showed that PI and RI were ≥1.35 and ≥0.73 respectively in malignant lymph nodes which indicated malignancy. Therefore it can be said that PI and RI could be helpful in differentiating malignant from benign lymph nodes. In a study by Shirakawa et al the mean of RI and PI in metastatic tumors were reported as more than benign tumors. Based on their results PI>1.3 and RI>0.72 indicate malignancy [11]. In a study by Na et al. PI and RI were specific for malignant lymphadenopathies. They determined cutoff points 0.8 for RI and 1.5 for PI in malignant lymph nodes, sensitivity was 100% and specificity for both were 47% and 55% respectively. They also concluded that unlike benign tumors 98% of malignant tumors have different pattern of blood supply [6].

In a study by Choi et al. mean and standard deviation of RI for malignant lymph nodes was 0.92±0.23 and for benign lymph nodes it was 0.52±0.11. They concluded that Spectral Dopller Ultrasonography is able to differentiate malignant nodes from benign nodes with high accuracy. Their findings were in consistent with our study [7].

CONCLUSION

Based on our results the color Doppler criteria in combination with gray scale ultrasonography could be helpful to select patients for biopsy or Fine Needle Aspiration (FNA), but cannot fully replace pathological evaluation.

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