Research Article

Role of ultrasound and color Doppler in evaluation of cervical lymphadenopathy

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Abstract

Background: Cervical lymphadenopathy is a commonly encountered clinical problem. Patients either present with palpable neck masses or with malignancy of the head and neck where the preoperative detection of the involved nodes is essential. Ultrasound and color/power Doppler are used to localize the node and evaluate their multiplicity, size, shape (roundness index), hilum status, margin, calcification, necrosis (>3 mm), and perilymphnodal edema. Color and power Doppler is used to know the pattern of vascularity and doppler indices [resistive index (RI) and pulsatility index (PI)].

Aims and Objective: To determine the role of ultrasound and color/power Doppler in the differentiatiation of benign and malignant nodes and in tapering the differential diagnosis.

Materials and Methods: Eighty lymph nodes were evaluated with ultrasound and color Doppler and correlated later with histopathology reports over a period of 18 months (May 2013 to November 2014) referred to Department of Radiology at Katuri Medical College and Hospital. Roundness index (<2), ill-defined margins, absence of hilum, peripheral/mixed vascularity, RI > 0.8 ,and PI > 1.5 were the criteria taken to diagnose the malignant involvement of the lymph node.

Results: Of the 80 lymph nodes examined, 22 are proved to be malignant on histopathology examination. Features such as roundness index, absence of hilum, and vascular pattern demonstrated sensitivities of 91%, 86%, and 86% and positive predictive values (PPVs) of 71%, 73%, and 86%, respectively. Among these features, pattern of vascularity and Doppler indices showed high PPV.

Conclusions: Ultrasound and color Doppler findings of roundness index, absence of hilum, vascular pattern, and impedance values revealed good PPV, sensitivity, specificity, and accuracy reaching 90% in differentiating benign from malignant lymph nodes.

KEY WORDS: Ultrasound, color doppler, cervical lymphadenopathy, benign, malignant

INTRODUCTION

Lymph nodes are secondarily involved in a variety of systemic diseases, local injuries, and infections. They are also the site of some important primary neoplasms and metastasis. Causes of cervical lymphadenopathy are inflammatory, infective (viral, bacterial, and protozoan), and neoplastic.

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The diagnosis of malignant lymphadenopathy is crucial for therapeutic planning in patients with suspected malignant neoplasm and for pretreatment staging in patients with primary malignant tumors of the head and neck. In patients with proven head and neck carcinomas, the presence of a unilateral metastatic node reduces the 5-year survival rate by 50%, whereas the presence of bilateral metastatic nodes reduces the 5-year survival rate to 25%.[1–3]

The histologic variations observed in lymph nodes in patients with nodal diseases are used to describe the morphologic changes in lymph nodes shown by gray-scale sonography.[4] High-resolution ultrasound is a useful imaging tool for the assessment of cervical lymph nodes because of its high image resolution and high sensitivity (98%) and specificity (95%) when combined with fine-needle aspiration cytology (FNAC).[5–7] Moreover, ultrasound is noninvasive and easily available. Therefore, it is suitable for both monitoring

Table 1: Classical criteria for differentiating malignant and benign lymphnodes

B scan criteria	Benign	malignant
Size	Small	Large
Shape	Oval	Rounded
Hilum	Present	Absent
Echogenicity	Moderate or low hypoechoic	Marked
Margins	Sharp	Irregular, blurred, angular, invasive
Structural changes		
Focal cortical nodules	–	–
Intranodal necrosis	Absent	Present
Reticulation	–	–
Calcification	–	–
Matting	–	–
Soft tissue edema	May be present	Absent
Doppler criteria		
Flow	Absent	Present
Vessel location	Central	Peripheral
Vascular pedicles	Single	Multiple
Vascular pattern	Regular	Chaotic
Impedance values	Low	High

disease progression and follow-up assessment after treatment. In proven metastatic nodes, size reduction on serial examinations is a useful indicator for monitoring patient's response to treatment.[1]

In addition to the gray-scale changes, both the angioarchitecture and the hemodynamics differ among various cervical nodal diseases. Neoplastic infiltration destroys the internal nodal architecture, which leads to the deranged morphology of the blood vessels in metastatic nodes, whereas local humoral agents causes dilatation of intranodal vessels in inflammation.

All these intranodal vascular changes help to differentiate benign and malignant lymph nodes.[8,9] The presence of intranodal vascularity, its distribution, and estimates of the intravascular resistance and spectral Doppler analysis are evaluated with color Doppler.

Cervical lymph nodes, which have the advantage of being located superficially, can be studied with even better spatial resolution. These classical criteria to differentiate the benign and malignant nodes described in Table 1 are applicable everywhere but they are studied on neck nodes.[1,5,10–16]

MATERIAL AND METHODS

This is a prospective study involving 80 lymph nodes from 72 patients of which 8 were known cases of head and neck carcinomas who were evaluated with ultrasound and color Doppler over a period of 18 months (May 2013 to November 2014) referred to Department of Radiology at Katuri Medical College and Hospital and later correlated with histopathology. In seven of the eight known malignancies, more than one lymph node was sampled, that is, 15 lymph nodes were sampled. Totally, 80 lymph nodes were studied. Patients aged 18 to 75 years of both sexes were included in this study. Ultrasound of the neck was performed after obtaining informed consent by using PHILIPS Envisor-C, high-resolution linear array probe at 3–12 MHz.

Ultrasound features documented included lymph node site, number, size, roundness index, presence and absence of hilum, margins of lymph node (i.e., well defined, ill defined, and matted), infiltration to adjacent structures, calcification, necrosis and cystic change, and perilymphnodal edema. Color Doppler and power Doppler features documented were the absence of vascularity, central vascularity, peripheral vascularity, and mixed vascularity. Spectral waveforms were taken from the intranodal vessel to document the Doppler indices: resistive index (RI) and pulsatility index (PI).

The criteria for the diagnosis of malignancy are size more than 10 mm, round lymph node (roundness index is calculated by the maximum dimension of lymph node to the minimum dimension no <2),[10,11] and absence of hilum. Color and power Doppler criteria for the diagnosis of maligancy are peripheral and mixed vascularity of the lymph node,[15] RI more than 0.8, and PI more than 1.5.

Other features documented were necrosis, calcification, and perilymphnodal edema. However, the significance of these findings in relation to malignancy is questionable becasue India is an endemic area to tuberculosis and to other infections and there has been an increasing incidence of infections among the immunocompromised patients. Acute suppurative involvement may be associated with perilymphnodal edema.

These features were compared with the histopathology reports obtained by FNAC or from the specimens of surgical dissection. From the data obtained, the positive predictve value (PPV), negative predictive value (NPV), sensitivity, specificity, and accuracy of the each finding was calculated.

RESULTS

The individual criteria for malignancy on ultrasound and color Doppler were compared with the histopathological findings (Table 2).

Size

Short axis diameter of more than 10 mm was taken as the criteria for enlarged lymph node. Of the 80 lymph nodes studied, 70 were greater than 10 mm, of which 20 were found to be malignant on histopathology examination. Of the remaining 10 nodes, two turned out to be malignant on histopathology. When considered alone, size criteria showed a PPV of 28%, NPV 80%, sensitivity 91%, specificity 14%, and accuracy 35%.

Shape (Roundness Index)

Benign nodes are either oval or elongated, and malignant nodes are often described as round in shape. To define the

Table 2: Different criteria and their significance

Ultrasound and color Doppler characteristics	Criteria	No. of Patients having ultrasound and color Doppler features	Histopathology for malignancy						
			Positive	Negative	Positive Predictive Value	Negative Predictive Value	Sensitivity	Specificity	Accuracy
Size	< 1.0 cm	10	2	8	28	80	91	14	35
	> 1.0 cm	70	20	50					
Roundness index (L/T)	> 1.5	52	2	50	71	96	91	86	87
	<1 .5	28	20	8					
Hilum	Present	54	3	51	73	94	86	88	88
	Absent	26	19	7					
Margins	Well defined	68	16	52	75	76	27	96	76
	Ill defined	8	6	2					
	Matted	4	0	4					
Calcification	Absent	74	22	52	0	70	0	90	65
	Present	6	0	6	100[a]	70	21	100	72
Perilymphnodal edema	Absent	75	21	54	20	72	5	93	68
	Present	5	1	4	80[a]	72	16	98	72
Necrosis	Absent	73	20	53	28	73	09	91	68
	Present	7	2	5	71[a]	72	20	96	68
Pattern of vascularity	Absent/central	57	3	54	86	95	86	95	92
	Peripheral	21	18	3					
	Mixed	2	1	1					
Doppler indices (RI)	<0.8	56	3	53	79	95	86	91	90
	>0.8	24	19	5					
Doppler indices (PI)	<1.4	59	4	55	86	93	82	95	90
	>1.4	21	18	3					

[a]Sensitivity, specificity, and other values for calcification, necrosis, and perilymphnodal edema are calculated for both presence and absence for diagnosis of malignancy and benignity.

nodal shape, the ratio between the longitudinal axis (L) of the node and the nodal transverse or short axis (S) is used, which is also known as axial diameter. The long axis of an oval benign node will be at least two times greater than the axial diameter, where the value of ratio will be L/S > 2 or S/L < 0.5.[10,11] In malignant (rounded) nodes, the value of L/S is less than 2 or even <1.5 or S/L > 0.5.[1,11,14] This ratio of long axis diameter to short axis diameter is called the roundness index.

Twenty-eight of the 80 lymph nodes showed a roundness index of less than 2, of which 20 lymph nodes were positive for malignancy. Rest of the 52 lymph nodes revealed a roundness index of more than 2, of which 2 lymph nodes were positive for malignancy. Roundness index criteria possesed a high PPV of 71%, NPV 96%, sensitivity 91%, specificity 86%, and accuracy 87%.

Hilum

Normal and reactive nodes show a central echogenic hilum interrupting the continuity of the cortex and continuing with the perinodal fat tissue (Figure 1). This appearance is because of the interface created by the subsurface of multiple medullar sinuses.[1,11,14] It has been shown that an echogenic hilum can be observed in about 90% of benign cervical nodes with a diameter more than 5 mm.[1] Malignant nodes generally show no visible hilum.[1,11,14,17] The absence of an echogenic hilum owing to replacement or effacement is considered to represent diagnostic criteria of abnormality and is significantly greater in malignancies than in benign lesions.[18,19] In malignant infiltration of lymph node, hilum is distorted and absent. Among the 26 lymph nodes that showed absence of hilum, 19 were positive for malignancy on histopathology examination and 3 of the 54 lymph nodes with normal hilum showed malignancy. Absence of hilum has a high NPV of 94%. The PPV, sensitivity, specificity, and accuracy were 73%, 86%, 88%, and 88%, respectively.

Margins

Acute inflammatory nodes possess blurred margins. Irregular or angular nodal margins lead to suspicion of metastasis.[20] Similar to Frank invasive contour, irregular and blurred margins indicate extracapsular and extranodal spread of malignancy and bear a severe prognosis.[1,11] Malignant nodes with sharp margins can also be observed.

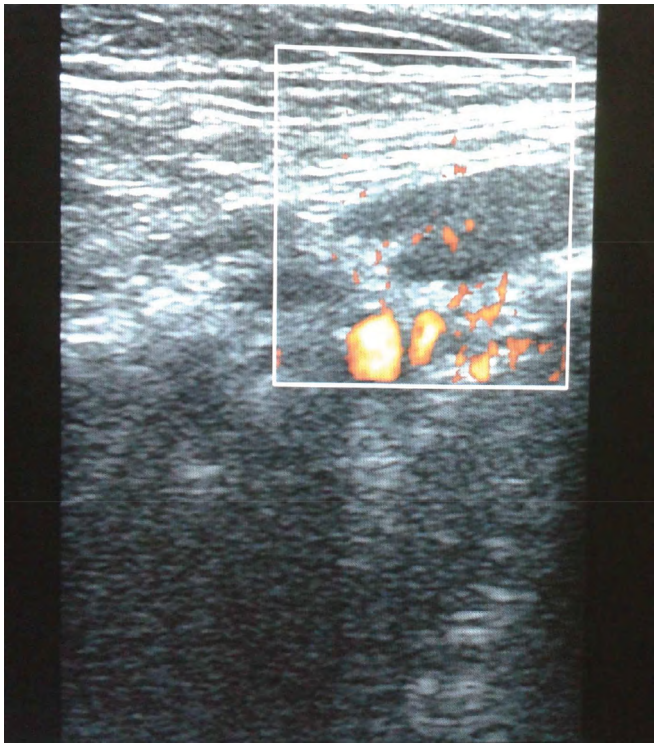

Figure 1: Normal lymph node, oval in shape (roundness index > 2) showing echogenic hilum, which is continuous with perinodal fat.

In these cases, tumor infiltration leads to high impedance mismatch.[1] Six of the eight lymph nodes with ill-defined margins were malignant on histopathology findings. Of the remaining, 68 showed well-defined margins and 4 matted margins; of these, 16 were positive for malignancy on histopathology examination. Ill-defined margins as criteria showed a high specificity of 96% and low sensitivity of 27%. The PPV, NPV, and accuracy were 75%, 76%, and 76%, respectively.

Calcification

Both papillary and medullary thyroid carcinomas show punctuate and peripheral microcalcifications, which appear as shadows only at high resolution.[1,11] They result because of calcification of infarcted tips of malignant papillae or intravascular tumor thrombi by psammoma bodies.[21,22]. Secondary carcinomas from papillary carcinoma of thyroid will show punctate calcifications in lymph nodes. Chronic infectious diseases such as tuberculosis and lymphomas after treatment will reveal calcifications in lymph nodes. In our study, only six lymph nodes showed calcifications. Assuming the presence of calcification to be malignant will have a low PPV of 0% and sensitivity 0% and high specificity 90%, whereas taking the criteria for benignity will have a high PPV of 100% and specificity 100% and low sensitivity 21%.

Necrosis and Cystic Change

Intranodal necrosis is of two types: coagulative and cystic necrosis. On ultrasound examination, a necrotic focus of more than 3 mm can be detected. Differentiation between the two types of necrosis is possible only when the focus of necrosis is large. Coagulation necrosis can be seen as an echogenic focus with no shadow, and it reveals no contact with the hilum or continuity with perinodal fat.[1,11] This necrosis can be observed in tuberculous nodes as well. Hence, it is just a sign of certainty for pathologic changes but without disease specificity. Cystic or liquefaction necrosis forms areas of eccentric fluid inside the lymph node structure. In the cases of papillary thyroid carcinoma, a cystic lymph node detection by ultrasonography suggests the presence of locally metastatic disease.[21,23] In this study, seven lymph nodes showed necrosis on ultrasound of which only two were positive for malignancy. Necrosis as a criteria for malignancy revealed a PPV of 28%. In developing countries such as India where the prevalence of infectious disease is high, necrosis can be seen as a part of infections. In this regard, considering necrosis as benignity will have PPV of 71%.

Perilymphnodal Edema

Perilymphnodal edema is usually the result of inflammatory reaction around the lymph node or caused by aggressive spread of lymphomatous/cancerous cells beyond the lymph node to the surrounding structures. In our study, five lymph nodes showed perilymphnodal edema of which only one lymph node revealed malignant deposits on histopathology examination. Assuming perilymphnodal edema as criteria of malignancy gives a PPV of 20%, whereas considering it as a criteria for inflammation, that is, benignity, results in a PPV of 80%.

Pattern of Vascularity

Lymph nodes possess a central main stump of vascularity in the hilum and small branches that taper near to hilum itself (Figure 2). In reactive hyperplasia of nodes, this pattern of vascularity is maintained.[15] Malignant deposits will reach the lymph node through the afferent lymphatics, which enters through the cortex; so, these deposits will rest near the cortex with neovasculrisation, resulting in peripheral or mixed vascurlarity (Figure 3). In our study, 21 lymph nodes showed peripheral vascularity and 2 lymph nodes showed mixed vascularity. Of these, 19 were positive for malignancy on histopathology examination. Peripheral and mixed vascularity has a PPV of 86%, NPV 95%, sensitivity 86%, specificity 95%, and accuracy 92%.

Doppler Indices

Resistive Index: Malignant cells infiltrate the lymph node, distorting its normal architecture and blood vessel morphology, thereby causing high-resistance flow patterns with RI of more than 0.8. In our study, 24 lymph nodes revealed a RI of more than 0.8, of which 19 were positive for malignancy on histopathology examination. RI possesed a PPV of 79%, NPV 95%, sensitivity 86%, specificity 91%, and accuracy 90%.

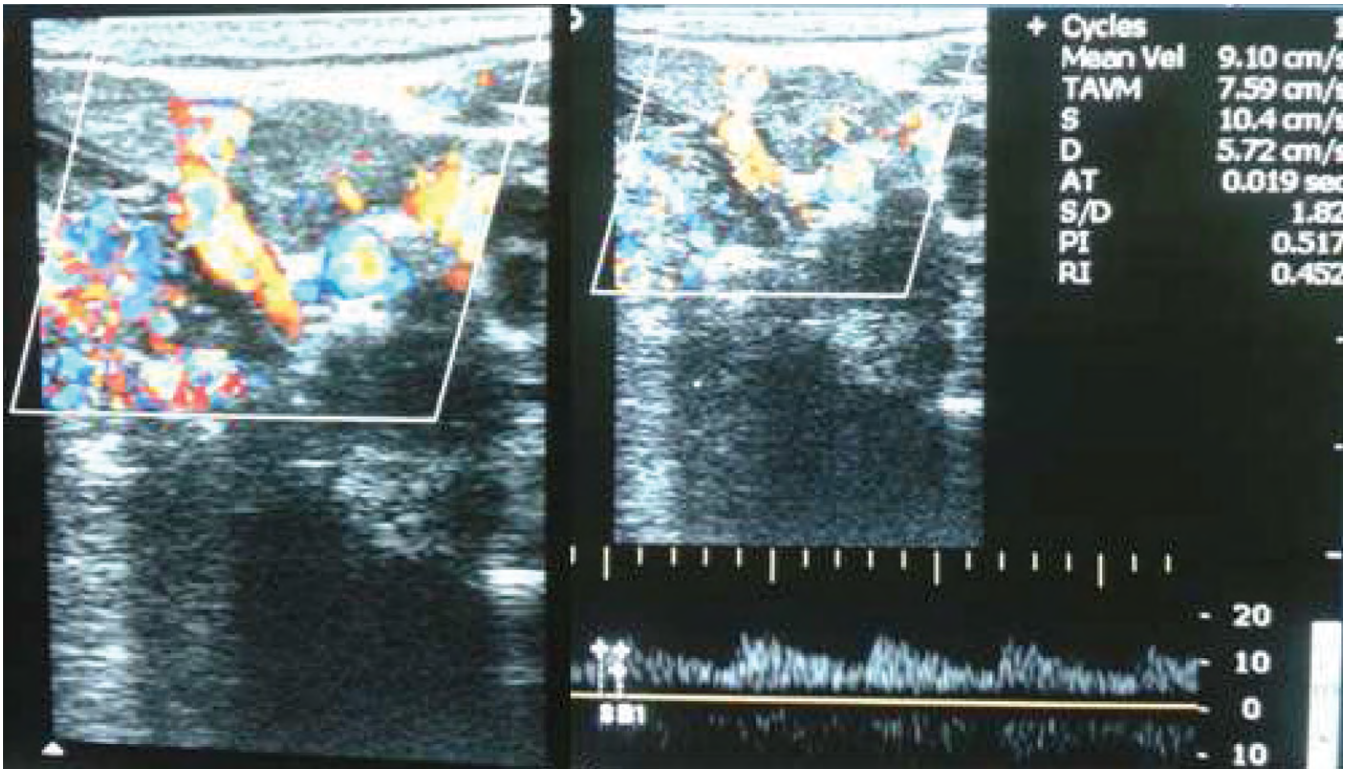

Figure 2: Enlarged lymph node with central vascularity and low Doppler indices which was benign on histopathology examination.

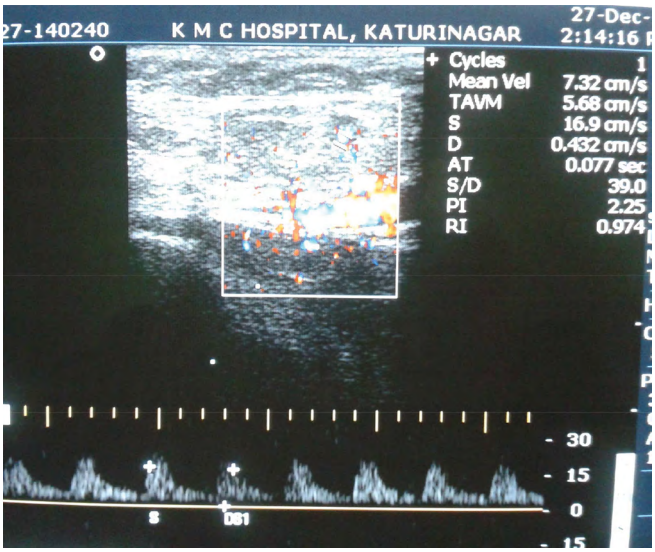

Figure 3: Enlarged lymph node with mixed vascularity and high Doppler indices, which was malignant on histopathology

Pulsatility Index: Similarly, along with RI, PI also increases in malignant nodes. PI of more than 1.5 is taken as a criteriion for malignancy. In our study, 21 lymph nodes showed a PI of more than 1.5 of which 18 were positive for malignancy. PI possesed a PPV of 86%, NPV 93%, sensitivity 82%, specificity 95%, and accuracy 90%.

DISCUSSION

Lymphadenopathy results from a variety of causes such as malignant deposits, lymphomas, infections, and other unusal causes such as autoimmune diseases. Accurate detection is helpful for staging and treatment planning.

A total of 80 lymph nodes from 72 patients were evaluated using gray-scale and colour Doppler ultrasound and compared with the histopathology findings. Of the 72 patients, 8 cases were known cases of malignancy of the upper aerodigestive tract and thyroid. In seven of the eight patients with known malignancies, more than one lymph node was sampled, that is, 15 lymph nodes were sampled, of which 12 turned out to be malignant on histopathology.

Of the 80 lymph nodes, 22 lymph nodes showed malignant deposits on histopathology examination. No case of lymphoma was observed in our study. Of the 58 benign lymph nodes, 33 were diagnosed as tuberculosis and 13 as reactive hyperplasia, and the rest were because of nonspecific inflammatory causes.

Table 3: Reliability of ultrasound and color Doppler based on kappa statistics

Property under study	*k* value	Strength of agreement
Size	0.046	Poor
Roundedness	0.711	Good
Hilum	0.703	Good
Margins	0.297	Fair
Calcifications	0.134	Worse than that expected to be seen by chance alone
Perilymph Node Edema	0.031	Worse than that expected to be seen by chance alone
Necrosis	0.006	Poor
Pattern Of Vascularity	0.784	Good
R.I	0.756	Good
P.I	0.777	Good

The criteria of roundness index, absence of hilum, ill-defined margins, peripheral and mixed vascularity, and high-resistance Doppler indices revealed significant specificity and sensitivity of more than 90%.

Dangore-Khasbage et al.[24] in a prospective study evaluated 70 cervical lymph nodes in 30 patients with known primary oral cancer using color Doppler ultrasound (CDUS) during a period of 8 months and the CDUS evaluation was found to be highly significant with a sensitivity of 92.9% and a specificity of 84.21%, after comparing the CDUS findings with Histopathological examination (HPE) results.[24]

Tschammler et al.[25] in their study found a specificity of 77% and a sensitivity of 96% of CDUS examination. In the study by Genes et al.,[26] the shape of lymph node and vascular pattern revealed a sensitivity of 84.21% and 97.37% and PPV of 82.05% and 82.84%, respectively.[26]

In our study, the features such as roundness index, absence of hilum, and vascular pattern demonstrated sensitivities of 91%, 86%, and 86% and PPV of 71%, 73%, and 86%, respectively. Among these features, pattern of vascularity and Doppler indices showed highest PPV. All these features show good reliability on kappa statistics (Table 3).

CONCLUSIONS

This prospective study showed good correlation between ultrasound and color Doppler with histopathology findings in differentiating benign and malignant lymph nodes, especially from roundness index, absence of hilum, vascular pattern, and Doppler indices. All these revealed good PPV, sensitivity, specificity, and accuracy, reaching 90%.

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