

# Usefulness of Hemodynamically Distribution of Intranodal Vessels in Differentiating Metastatic Neck Lymph Nodes – Value of Color Doppler and Spectral Wave Sonogram

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## ABSTRACT

**Objective:** To evaluate the diagnostic assessment of enlarged lymph nodes, based on its perfusion pattern by taking tissue diagnosis as gold standard.

**Study Design:** Analytical study.

**Place and Duration of Study:** Departments of Radiology and Pathology, PIMS Hospital, Islamabad, from February to May 2016.

**Methodology:** Color sonography of patients with clinically, palpable cervical lymph nodes were carried by senior trainee under the supervision of senior radiologist. Ultrasound guided tissue diagnosis was obtained in all suspected malignant cases. Histopathology was taken as the gold standard for determining accuracy.

**Results:** Accuracy, sensitivity and specificity, positive and negative predictive values of color Doppler ultrasound in detecting malignant cervical lymphadenopathy was found to be 88.46%, 86.05%, 79.31% and 92.50%, respectively with diagnostic accuracy of 86.95%, when intranodal vascular pattern on color Doppler imaging was analyzed. Using spectral wave indexes, the same values were 92.31%, 90.70%, 85.71%, 95.12%, respectively with overall diagnostic accuracy of 91.30%.

**Conclusion:** Color Doppler sonography is much sensitive borderline than grey scale findings alone. Furthermore, lymph nodes appearing in the detection of malignant nodes on grey scale images can be reliably diagnosed on Doppler scan.

**Key Words:** *Metastatic lymph nodes. Color Doppler. Vascularity. Spectral indexes.*

## INTRODUCTION

Head and neck cancer is one of the most devastating cancers, often leaving the patient disabled and disfigured and also affecting the crucial function of life like breathing, eating and smelling.<sup>1</sup> Neck status is the single most important indicator of prognosis in these patients. The involvement of the lymph nodes with metastatic deposits is always associated with a poor prognosis, approximately 50% poorer than for patients with equivalent tumors with no nodal involvement. So, early detection of lymph nodes involvement has great therapeutic and prognostic implications in these patients.<sup>2,3</sup>

Tumor angiogenesis plays a critical role in determining tumor size and its regional and distant tumor spread, consequently effects management and prognosis of these patients.<sup>5</sup>

High-resolution ultrasound is an invaluable diagnostic imaging for these metastatic lymph nodes due to its high image resolution, non-invasiveness and easily availability along with its highly valuable color and Doppler resistive index (RI) and pulsatility index (PI) value.<sup>3,6-12</sup> Metastatic lymph nodes are reported to have higher resistivity index (>0.8) and pulsatility index (>1.5) than reactive lymph nodes.<sup>7</sup> Previous results showed a sensitivity, specificity and diagnostic accuracy for malignant nodal involvement as 55%, 100%, and 74%, respectively, with a cutoff value of 1.5 for P1 and accuracy of 70% with cutoff value of 0.8 for RI.<sup>13</sup>

The objective of this study was to evaluate the diagnostic accuracy of color Doppler sonography in differentiating benign from malignant lymphadenopathy, based on its vascular pattern and spectral waveform analyses using histopathology as the gold standard.

## METHODOLOGY

It was an analytical study conducted in PIMS Hospital from February to May 2016 with the permission of the Ethical Committee of the PIMS Hospital.

Patients of either gender aged 40-80 years, having clinically palpable cervical lymphadenopathy, were included. Patients with histopathologically proven cancers were excluded. All patients were scanned in supine position with slightly extended neck with color

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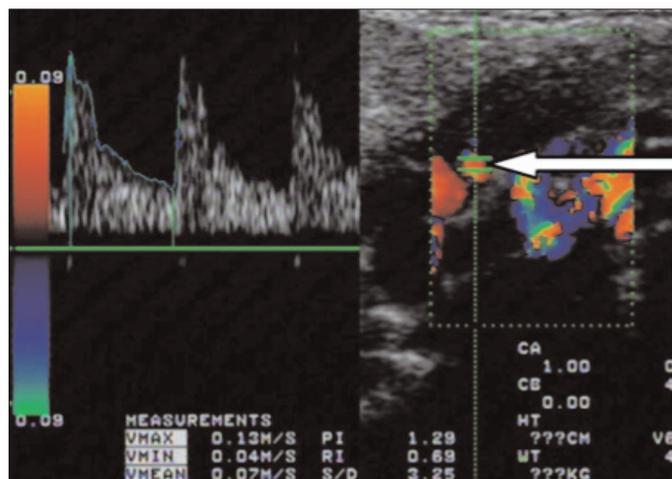


Figure 1: Color Doppler scan along with spectral waveform showing peripheral flow pattern with high RI and PI typical for malignant cases.

Doppler sonography, using a 5- to 10-MHz linear array transducer, positioned on the surface of the neck to avoid artifactual increase in vascular resistance secondary due to compression of nodes. Scan was performed by a senior fellowship trainee under the supervision of a qualified radiologist with optimized color Doppler parameters for maximum visualization of blood vessels.

Based on the studied parameters (vascular pattern and waveform), scanned lymph nodes were categorized into two groups. First, hilar vascularity patterns were categorized in three groups: absence of central vessels with eccentric or peripheral distribution, abnormal multifocal pattern and deformed/aberrant radial configuration of vessels in involved nodes (Figure 1).

Second group was categorized based on perfusion pattern along with maximal peak systolic velocity (PSV), end diastolic velocity (EDV), resistive index (RI), and pulsatility index (PI) were calculated for each node. Doppler spectral waveforms were analyzed for the three different vessels for each node and the highest value was considered. Cutoff value of Doppler indices were RI=1.0 and PI=1.5, and one of the abnormal vascular pattern was used for categorizing lymph node as metastatic.

Color Doppler and spectral waveform findings were compared with histologic findings. Statistical analysis was made using SPSS version 16. Mean and standard deviation was calculated for quantitative data and frequency with percentages for qualitative data. Sensitivity, specificity, positive and negative predictive values were calculated by using 2x2 contingency table.

### RESULTS

A total of 69 (both genders of 40-80 years) patients included in this study, 39 (56.52%) were male with mean age of 60 ±10.3 years and 30 (43.47%) were female with mean age of 58 ±12.8 years.

Table I: Distribution of PSV and DV among malignant and benign lymph nodes.

Lymph node type	Statistics	PSV (cm/sec)	DV (cm/sec)
Malignant lymph nodes	Range	4-35	-7 to +7
	Mean ±SD	22.52 ±6.16	1.03 ±3.53
	Median *	23.00	2.00
	Interquartile range*	20.50-25.0	-2 to +3
Benign lymph nodes	Range	8-75	3-45
	Mean ±SD	30.33 ±13.02	11.63 ±10.10
	Median *	28.00	8.00
	Interquartile range*	22.0-36.75	5-14.75

\* Median and interquartile range has been reported because both PSV and DV do not follow the normal distribution.

Table II: Distribution of RI and PI among malignant and benign lymph nodes.

Lymph node type	Statistics	RI	PI
Malignant lymph nodes	Range	0.9-1.7	1.5-2.0
	Mean ±SD	1.00 ±0.15	1.7 ±0.15
Benign lymph nodes	Range	0.4-0.7	0.3-1.2
	Mean ±SD	0.52 ±0.12	0.72 ±0.28

Table III: Validation parameters of color Doppler and spectral Doppler taking FNAC as gold standard.

Validation parameters	Color Doppler	Spectral Doppler
Sensitivity	88.46%	92.31%
Specificity	86.05%	90.70%
Positive predictive value	79.31%	85.71%
Negative predictive value	92.50%	95.12%
Diagnostic accuracy	86.95%	91.30%

In 29 (42%) patients, cervical nodes were found malignant on color and spectral waveform pattern, and remaining 40 (57.97%) showed benign appearance. The malignant-looking nodes were correlated on histopathologically later on. Twenty-three (79.31%) of them (n=29) proved to be malignant and 6 (20.68%) were benign (false positive on color coded images). All these false positive cases showed aberrant vascular distribution that favors for their malignant potential and 3 (50%) out of them (n=6) showed suspicion for malignancy due to Doppler indexes that fell in the range of metastatic involvement.

Three (7.5%) out of the remaining 40 benign appearing lymph nodes looked suspicious on color Doppler. However their spectral indexes and later on decrease in sizes favored their benign nature. The remaining 37 (92.5%) showed normal pattern on images based on perfusion pattern as well as on spectral waveform indexes, along with physical examinations and clinical manifestations so all of these were placed on follow-up. Managed conservatively, later they showed a reduction in size on follow-up scans, potentiating their benign nature.

They had shown a normal central location of hilar vascularity which was radially symmetrical. Aberrantly, vascularity was observed in only 3 (7.5%) out of (n=40)

benign reactive nodes, which were explained gross nodal necrosis, and vasculitis secondary to gross inflammation in these cases. Eccentric/peripheral vascularity with loss of hilar vascularity were observed in 25 (86%) out of the 29 malignant cases, deformed radial pattern in 1 (2.5%) and aberrant multifocal pattern in 3 (7.5%).

Velocity value and variation is given in Table I. RI and PI were  $1.00 \pm 0.15$  and  $1.7 \pm 0.15$  for malignant lymph nodes; and  $0.52 \pm 0.12$  with PI of  $0.72 \pm 0.28$  for benign group, respectively (Table II). The sensitivity, specificity, positive predictive value and negative predictive value in our population were calculated with the help of these 2x2 tables and were found to be 92.31%, 90.70%, 85.71%, 95.12% with overall diagnostic accuracy of 91.30%, respectively. The statistical analyses, based on distribution of intranodal vessels, show sensitivity, specificity, positive predictive value and negative predictive value (Table III).

## DISCUSSION

Anatomically, a normal lymph node has both an arterial and a venous systems. The arterial system consists of a hilar nodal artery, smaller arteries or arterioles in the medulla and trabecular structures, and sinuous capillaries in the cortex branched from arterioles entering the cortex. A few arterioles reach the capsule *via* trabecular structures. The veins generally parallel the arteries. This histologic vascular anatomy of the lymph node explains the normal pattern of nodal vascularity that appears as radial with symmetric distribution.<sup>14</sup>

Various studies, based on grey scale morphological criteria of lymph nodes, did not show promising results for differentiation between benign and malignant cases, suggesting that confirmation on tissue diagnosis has to be made for managing these patients.<sup>9,11</sup> Color Doppler sonogram along its spectral waveform analysis improves the accuracy of ultrasound in benign and malignant cases. Inflammation causes dilatation of vessels and metastatic spread induces compression of these vascular structures, which correspondingly decrease and increase the vascular resistance which are basis of this imaging modality for differentiation. Architectural distortion along with neoangiogenesis explains this phenomenon in malignant cases with preservation of normal vascularity pattern in benign cases.<sup>15</sup>

In this study, the pattern of central vascularity was dominant in benign reactive nodes; whereas, the most common pattern was absence of central vascularity along with eccentric/peripheral perfusion (86%) in malignant nodes which might be explained on the basis of tumor infiltration and tumor angiogenesis. However, some benign nodes showed variable abnormal vascularity patterns. This can be explained as some aggressive inflammatory processes end into total

necrosis and gross vasculitis along with vasodilatation, which may mimic aberrant vascular patterns. It was observed that some malignant looking nodes, which had aberrant/ deformed vascular pattern along with borderline spectral indexes of RI and PI, finally proved to be benign, thus makes some limitations in this study in lower range for these parameters.

Current experience data supports the results of several previous reports malignant nodes tend to have higher RI and P1 values than benign nodes.<sup>2,3,5</sup> However, PI and RI values in current study showed false positive results in 7.5% cases in the lower range of these indexes as is reported in previous studies as well. So, hilar vascular pattern along with grey scale morphology and follow-up improves accuracy in these cases.

The present results show that analysis of nodal vascularity pattern, along with waveform indexes, is very important in patients with cervical lymphadenopathy of suspected head and neck cancer for planning and managing these group of patients and preventing the benign looking lymph nodes from unnecessary invasive procedures like FNAC by putting these patients on follow-up scan; thus improving quality life of these patients and also contribute a lot in economic resources.

The authors succeeded in enrolling a large sample population with suspected metastatic cervical lymph nodes. Keeping in mind the financial constraints, along with less health facilities and services in the developing countries like Pakistan, high resolution ultrasound has an important role and may be continued as the first choice for the assessment of these metastatic lymph nodes.

The main limitation of this study is that this was a single center study; and like all single center trials, the results cannot be widely generalized, since data was also collected for limited duration and there has been no long-term follow-up of the study participants.

## CONCLUSION

Color Doppler sonography is more sensitive than grey scale findings alone in detection of malignant nodes. Furthermore, borderline lymph nodes on grey scale images, which are equivocal for malignant/benign nature, can be reliably diagnosed on this imaging scan, avoiding unnecessary tissue punctures, thus improving prognosis of these patients.

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