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Presurgical evaluation of malignant neck nodes by assessment it's Intranodal vascularity using the color Doppler ultra sound

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Abstract

Color Doppler ultra sound is an ideal imaging tool for initial assessment of intranodular vascularity which may reflect some pathological behaviors of tumors and lymph nodes in patients with cervical lymphadenopathy. The aim of this study was to evaluate the usefulness of Color Doppler ultra sound in differentiating benign from malignant cervical lymph nodes by the assessment of Nodal vascularity. In a prospective study of 24 untreated patient with 65 cervical lymph nodes clinically including enlarged hard and soft palpable and non palpable lymph nodes . All these lymph nodes were evaluated with Color Doppler ultra sound as a pre-surgical diagnostic tool, the findings were compared with histo-pathalogical results.

Fine needle Aspiration cytology was used for 15 palpable enlarged cervical lymph nodes, most of these lymph nodes 12 lymph nodes were associated with reactive lymph nodes and not operated on, just follow up with antibiotic treatment and performed only 3 lymph nodes were associated with malignant lymph nodes which removed surgically and assessed histopathologically.

Upon Color Doppler ultra sound examination pre-operatively of 65 cervical lymph nodes were found 20 lymph nodes as a reactive lymph nodes and 45 as malignant lymph nodes.

After neck dissection, all lymph nodes histo-pathologically examined which showed 22 benign lymph nodes and 43 lymph nodes containing metastases. Nodal vasculature were classified into:

- Hilar
- Capsular
- Hilar with capsular vascularity

Results: most of the malignant nodes showed the presence of capsular vascularity and capsular with hilar vascularity, 37.2% and 48.8% respectively, where as the majority of the reactive nodes showed hilar vascularity 77.3% and the different was highly significant $P<0.01$ when chi-square was used.

Conclusion: the distribution of intra nodal vascularity appears to be useful in differentiating benign from malignant cervical lymph nodes by means Color Doppler ultra sound which consider as a routine pre-surgical tool to provide the surgeons with a valuable information that aids them to modify their surgical management.

Introduction

In the treatment of patient with head and neck cancer, the surgeons aims to cure the patient by surgical removal the diseased tissue [1]. Traditionally cervical lymph nodes (CLNs) in the neck have been assessed clinically according to TNM system classification for the detection of any palpable node howoever (1cm in size)one billion tumor cells present metastatic disease which easily missed on this clinical examination [2].

Clinical examination of neck for lymph nodes (LNs) has a low sensitivity and specifity with false negative results that range from 15% to 25% [3,4].

Palpable neck lymph nodes are commonly seen in many patients with cervical lymphadenopathy. This is because reactive hyperplasia of lymph nodes is strongly associated with inflammatory processes which commonly seen in about 90% of patients within 4-10 years which is also a clinical manifestation of malignancy present in the cervical lymph nodes [5, 6].

Management of neck metastatesis in patients with oral cancer is controversial subject among different examiners. Some clinicians and surgeons advocate elective treatment of the neck [7, 8].While others [9], still advocate a (wait and see policy) at lest, when no nodes are palpable.

Technological advances in radiology over the last decade have made computer tomography (CT), magnetic resonance imaging MRI and ultrasound 'US' are the primary tools for evaluating the head and neck cancer [10].

Histological changes in vascular structure in nodal disease are not well understood. Lymph nodes involved by malignant disease may have deformed vascular structure, due to distortion of normal nodal architecture by tumor infiltration and neo-vascularation induce by angiogenesis factor. Tumors secret a number of growth factors and proleolytic enzymes into the interstitium that act on endothelial cells and basement membranes to remodel existing vessels and stimulate the release of endothelial progenitor stem cell (EPSC) from bone marrow to form new blood vessels [11, 12]. Therefore the architecture and hemodynamics of nodal vessels would differ among various nodal diseases. This property provides the potential for diagnosis when vascular can be reliably detected.

Color Doppler ultrasound has been proposed as a method of differentiating benign from malignant lymphadenopathy [13]. In CDUS made it possible to visualize and assess intranodal vascularity and assess the vascularity of tumor, with high resolution real tissue US techniques to monitor Patten of blood flow vessels as small as these found in LNS [14, 15].

The vascularity of LN can be used as a criterions factor for malignancy evaluation in CDUS [16]. The presence of normal Hilary flow on Doppler sonograms was highly suggestive of non metastatic nodes.

The presence of extra hilar vessels is thought to be one signs of malignancy in the color duplex sonography of LNs even when the node is normal in size [15].

Hamid R, Latifiy, et al. [19]. classified nodal vascularity into 4 patterns:

1 - Peripheral pattern
2- Mixed pattern
3- Cental pattern
4- Absent blood flow.

WU. CH; Shihi J, et al.[20] classified nodal vascularity into 4 patterns:

1- Hilar type: only a simple or centrifugal branches.

2- Spotted type: scattered spots of vessel signals

3- Peripheral type: vascular signals distributed just around the node.

4- Mixed type: mixture of more than one type.

Na; Dong Gyn; et al [21] Divided the hilar vascular pattern into 3 groups, according to location of hilar vascularity: centric, eccentric, and absent hilar .

Also the central hilar vascularity assessed and 4 morphologic categories were assigned:

- The Radial vascularity:- which is symmetric under directional arte rid flow (from hilar to cortex).
- Deformed radial:- A symmetric radial vascularity
- Multifocal vascularity :- (more than 3 area) with loss of Radial flow. Only peripheral vascular can be see
- Absent vascularity:- no vascular sign.

So that abnormal pattern of nodal vascularity was seen in benign nodes and malignant nodes with a sensitivity 98% & specificity 63% for determination of metastatic node from non metastatic node vascularity. Ying M; Ahuga A; et al [22] Oktay A. MD, Efraan A, et al [23], Maremoniti P. Califano L; et al .[26]. determined the vascular patterns of LNs in to the following:

1. Central vascularity.
2. Peripheral vascularity.
3. Central + peripheral vascularity.
4. Absent vascularity.

Most of the metastatic nodes vascularity capsular and capsular and hilar but the majority of the reactive nodes showed hilar vascularity

Reactively enlarged node, Showed greater hilar perfusion where as metastatic showed midline of peripheral with central perfusions [14, 24, 25, 26].

Dorothee. R, Jecker P; et al. [27]. Classified the vascularity patterns into:

1. Hilar pattern: patterns in which vessels were limited to the hilum.
2. Heterogeneous pattern: in which vessels were distributed individually and diffusely over LN stroma.
3. Complete pattern: which the entire stroma was virtually filled with vessels.
4. Mixed pattern: in which the vessels were run from hilum to the LN periphery.

Reactive enlarged node showed greater hilar perfusion while metastatic node showed as peripheral, peripheral + central perifusion[23, 28].

Extra hilar vessels which entered through the surface & not through the hilus & considered a useful sign of malignancy[15].

Malignant LNs tend to have peripheral vascularity where as benign node usually have hilar vascularity[22,23,29].

Material and method

The research was carried out on 24 patients with a history of cervical lymphadenpathy were attending to the oral surgery department of AlKurk hospital prospectively.Upon physical examination of 65 CLNs, we found 56 palpable enlarged LNs, 30 LNs were found to be hard, 26 LNs were determined to be soft and 9 LNs were non palpable these were only noticeable under (CDUS) examination as shown in figure (2).

All of them had been subjected to (CDUS) examination without prior information about other diagnostic investigations or any surgical procedure or radiotherapy treatment.

A total of 65 lymph nodes were

controlled by either fine-needle. Aspiration cytology (FNAC) n=12 LNs were associated with reactive lymph nodes and not operated on, just follow up with antibiotic treatment and the others surgical pathology (n=53) LNs.

These LNs subjected to a histopathology examination and were found to be benign n=22 and malignant n=43 LNs.

All color Doppler sonographic procedures were done with a 7 to 10 MHZ linear array transducer (siemens sonoelegra line-Germany) by one an experienced radio-sonologist who unaware of the physical findings. We evaluated the vascularity of 65 LNs as:

- The hilar vascularity pattern: flow signals originate from the central region of LN.
- Capsular pattern vascularity: flow signals originate from the periphery of node .
- Hilar with capsular vascularity: flow signals presence at central and periphery regions of LN.

After surgical exsion of primary tumor with the neck dissection for removing 53 LNs from 15 patients. Each of these lymph nodes was evaluated by one pathologist histopathologically with an emphasis on the nodal blood vessels architecture and tumor neovascularity in malignant nodes.

Color Doppler ultrasongraphic findings were compared with histological findings. Chi-square test was used to calculate the significance of difference in vascular patterns between malignant and benign LNs. In addition to the four fold contingency table to assess the accuracy, sensitivity and specify of clinical with CDUS and histopathological findings.

Result and Discussion

This study was based on 24 patients with cervical lymphadenpathy 14 (58%) were male and 10 were female (42%) as shown in figure (1). The average age of a total group was 9-59 years. The mean average age (37.8) with SD= 15.24 as shown in table (1).

In table (2) the Correlating of physical examination results with the results of histopathologically study. 23 of palpable LNs were proved histopathologically to be malignant LNs while other's 7 palpable LNs were diagnosed histopathologically as benign LNs.

Regarding to the palpable soft and non palpable LNs which detected by CDUS and in the neck dissection we found that, 20 LNs were confirmed as malignant where as 15 LNs were proved to be benign LNs.

As a result of these data the clinical examination had an accuracy (58.46%) with sensitivity (53.48%) specificity (68%) .

This result comes in agreement with study [30] Who had moderate sensitivity and disagreement with other studies [31, 32] in reporting sensitivities higher than our study.The moderate sensitivity appears in this study was attributed to relatively less than half number of malignant LNs that were not detected by palpation. Concerning to the specificity .There is in agreement between this study specificity and those authors studies [30, 32] in reporting moderate and high specificities, and disagreement with other studies [33, 34] in reporting low specificities. The moderate specificity in this study reported due to large number of benign LNs that were correctly diagnosed by palpation which included the LNs that did not notice in clinical examination which considered benign LNs.

Color Doppler ultra sound is the only method that can display angio-architecture of LNs in daily practice and so it has been proposed as a

method of differentiating malignant LNs from benign LNs. This comes in agreement with many studies [21, 23, 27] who reported that it is at most important to recognize absolutely reliable criteria for malignancy when using imaging method. .According to researcher [6], who mentioned that evaluation of intra nodal vascular pattern of normal and abnormal cervical LNs using CDUS has been reported to be reliable with 85% where as our study disagree with author [23], who said that subjective findings such as nodal vascularity are not reliable tools for thyroid nodes evaluation. .

In this study, the nodal vascularity was assessed according to the distribution of blood vessels within cervical LNs and classified into 3 patterns only that were observed in the color Doppler ultra sound flow : hilar vascularity, capsular vascularity and capsular with hilar vascularity, our results are in agreement with those studies [6,14,28] in their classification to the nodal vascular patterns; hilar, capsular, hilar with capsular. and disagrees with others studies whose classified the nodal vascular patterns in other classification. Hilar spotted, peripheral and mixed according to the Wu. C.H: Chamg Y: Hsu, et al . [24] . A Central, peripheral, mixed and absent blood flow according to Hamid R, Latifiy, et al . [19]. Complete, heterogeneous, hilar and mixed according to Dorothee. R, Jecker P; et al . [27]. Hilar with it is division type I (normal hilar)and type II hypertrophichilar and the other peripheral pattern type III according to Giovagnorio F. et al. [29].

As in table (3) the hilar vascularity, capsular vascularity and capsular with hilar vascularity was seen in 35.4%, 21.5% and 43.1% of LNs respectively.

Among the malignant and benign LNs, 6.7% and 100% showed hilar vascularity respectively. While capsular and capsular with hilar vascularity was observed in only malignant nodes 31.1% and 62.2% for each. So we observed hilar flow signals in the benign LNs , this agrees with the [21] in that flow signals were detected as dot like pattern. and this comes in agreement with those authors [28,3,14]. In stating that the reactive LNs preserve their normal hilar vascular pattern while disagrees with the [14]. Who stated that malignant processes in LNs results in a more variable vascular pattern.

The malignant LNs showed in CDUS a highly vascularity in capsular and capsular with hilar regions than benign LNs which showed a highly vascularity in hilum region and the difference was a highly significant with the P value ($P<0.01$) when chi-square was used for statistical analysis .Our findings confirm the findings of those studies [2,14,3,5] who found that the presence of high intranodal vascularity has been used as a key feature to differentiate malignant from benign nodes and the difference was significant.

Table (4) shows the three patterns of nodal vascularity were observed by CDUS and correlated with histopathological results study which classified as a follow:

1. Hilar vascularity: the highly normal blood vessel can be seen limited within the hilum region of LNs this pattern was commonly observed in (77.3%) of benign LNS, while also were seen in (14%) of malignant LNs. Our results agrees with many studies [28, 13, 14] in their explanation in that the reactive node showed predominantly hilar vascularity due to increase in blood vessel diameter and blood flow, as a result to the diffuse nature of the histological process, occurring within the node is more likely to be preserve the

normal vascular pattern. In the present study, the low percentage of the malignant LNs have hilar vascularity due to that malignant node in the beginning stage has nearly similar artichitecture of reactive LN This was in agreement with the [37] in his explanation that early stage of microinfiltration vascularity may increase owing to local immune reaction. However, the original architecture of LNs is rarely altered.

2. Capsular vascularity: in which the pre-existing blood vessels were run from periphery to hilum of LNs this pattern was found in 16 malignant LNs (37.2%) while presented in 4 benign LNs (18.2%).In our study the malignant LNs had capsular vascularity may be due to the neosvascularization by tumor infiltration induces aberrant vassels at periphery of LNs. This confirms with those studies [27, 28, 38] in their explanation that the prominence of capsular vascularity at the periphery of malignant LNs appears secondary to initial deposition of carcinoma cells in marginal area. In capsule of some benign LNs ,this agrees with the [28]. In reporting that this dot caused by enlarged normal arterioles in the capsule of LNs.

3. Capsular with hilar pattern: in which the blood vessels distributed the whole LNs including hilum region and periphery region the type of pattern was almost found in 48.8% of malignant LNs while only one benign LNs (4.5%) was observed with this patterns. Also the malignant LNs had the highest percentage among the hilar with capsular vascularity pattern the main reason is that the malignant LN when reached advance stage inducing randomly new blood vessels to nitrate the tumor which is agreement with [21, 27] in their explanation that the late stage as the node is progressively involved with neovascularization by tumor infiltration lead to increase the vascularity at hilar and periphery of node due to inducing aberrant vessels. In the case of benign LN blood vessels appears at periphery and hiluim due to the proliferating distal branches of normal arterials and this can be mistaken for abnormal vascular pattern. This agrees with the [21]. Who found that the signals appears in capsular and hilar region of benign LN. Refer to the duration of illness.

Benign LNs mostly had a hilar vascularity while malignant LNs had the other 2 types of vascularity patterns.

Comparison between CDUS and histopathological results of 65 LNs are summarized in table (5).In this study the CDUS failure to distinguish only 2 LNs which is considered as malignant nodes but they proved histopathogically benign LNs. This may due to that the hilar with capsular vascularity in the LNs may be reached advanced stage of reactive LNs or early stage of malignant LNs that the micrometastasis remain occult with any technique. This agree with many studies [6, 36] who found vascular pattern of benign nodal disease vary with the duration of illness.

In our study the color Doppler ultra sound correlated with histopathological finding showed a highly significant difference in differentiating malignant from benign LN with P value ($P<0.01$), that the hilar vascularity pattern were commonly found in reactively benign LNs where as the second and third patterns were most often seen within malignant LNs this results comes in agreement with many studies [6, 14, 37] who seen hilar vascularity is usually found in reactive nodes whereas

peripheral or mixed vascularity are common in malignant nodes and disagree with authors [29, 39]. Who reported that malignant LNs has mostly capsular or peripheral vascularity. Also disagree with the [23] and, [39] who found that 90% of malignant nodes are mixed.

Conclusion

Color Doppler ultra sound imaging is clearly more sensitive than the surgeon fingers at detecting the non palpable LNs in cervical region that could not be found in clinical examination, the clinical examination is a poor method for detection LN metastasis and the CDUS can be consider as routine pre-surgical tool by providing the surgeons with valuable information which aids them to greatly modify the surgical management therefore color Doppler ultrasound results are readily applicable in routine clinical practice.

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Table (1): Descriptive of age group.

	Age
Mean	37.8
SD	15.24
Range	50

Table (2): evaluation of the validity of physical palpation for diagnosis of cervical LNs metastasis.

Physical palpation	**Histopathalogical examination**		
	No. of malignant L.N	**No. of benign L.N**	**Total**
+ve	23	7	30
-ve	20	15	35
Total	43	22	65

Accuracy = 58.46% Sensilivity = 53.48% Specificity = 68%

Table (3): vascular patterns of malignant and benign LNs detected by color Doppler ultrasound.

Nodal uascular	**Malignant nodes**		**Benign nodes**		**Total**	
Patterns	**No**	**%**	**No.**	**%**	**No.**	**%**
Hilar	3	6.7	20	100	23	35.4
Capsular	14	31.1	0	0	14	21.5
Capsular + Hilar	28	62.2	0	0	28	43.1
Total	45	100	20	100	65	100

*Chi-square=52.7 P<0.01 High significant

Table (4): The relationship between color Dopplor ultrasound nodal Vascular mapping classification finding and histo-pathological finding results.

Classification The Nodal Vascular	**No. of Malignant L.N=43**		**No. of Benign L.N =22**	
	No.	**%**	**No.**	**%**
Hilar	6	14	17	77.3
Capsular	16	37.2	4	18.2
capsular + Hilar	21	48.8	1	4.5
Total	43	100	22	100

*Chi-square= 26.6 P<0.01 High significant

Table (5): Comparison of results of color Doppler ultrasound and histopathology.

Modality	**No. of malignant nodes**	**No. of benign nodes**	**Total no. of LNs**	**Statistical analysis P -value**
CDUS finding	45	20	65	P <0.01 High significant
Histopathlogical finding	43	22	65	P<0.01 High significant

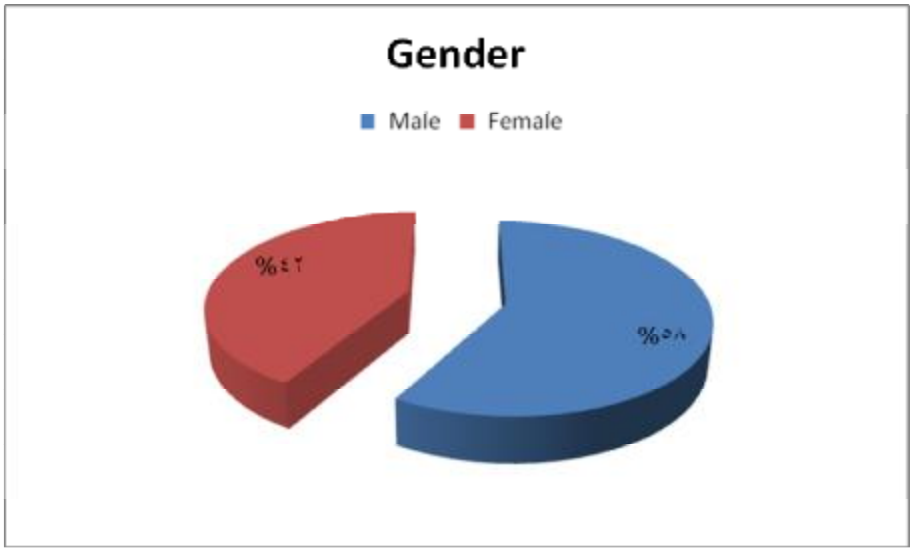

Figure (1): The pie chart shows the distribution of the study sample by sex.

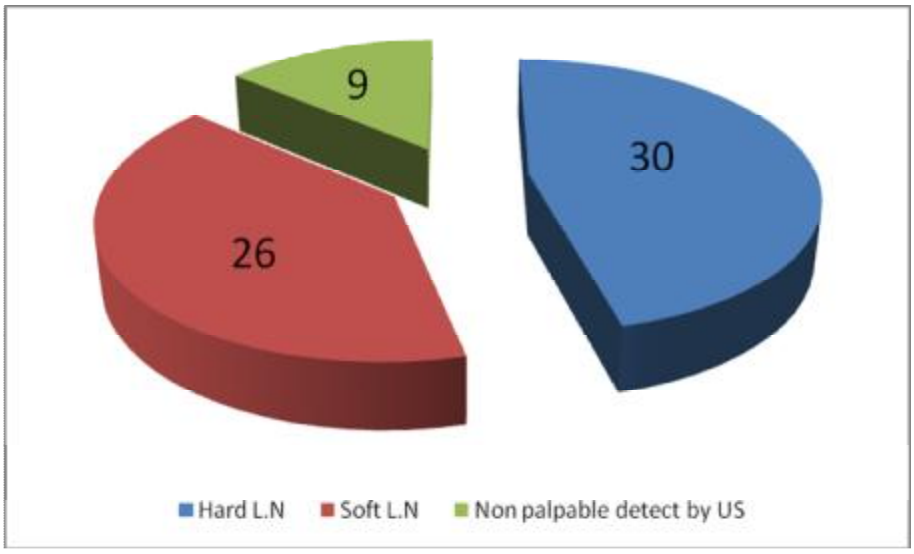

Figure (2): The pie chart shows the physical examination finding for cervical lymph nodes.

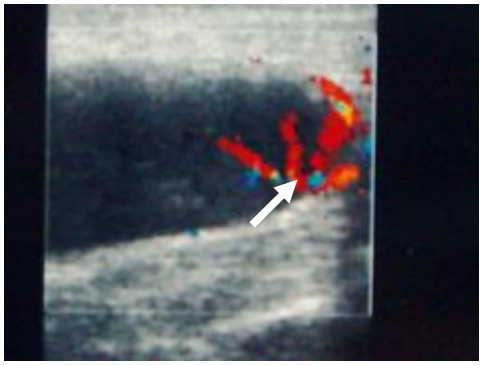

Fig (3): Color Doppler sonography: a transverse scanning of elongated submandibular Benign LN wi‘h hilar vascularity (white arrow)

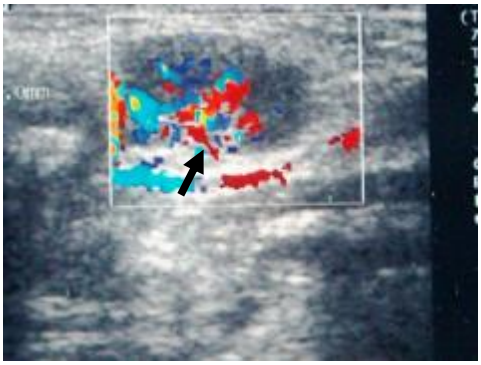

Fig (4): Color Doppler sonography, a transverse scanning of submandibular reactive benign LN, shows typical hilar vascularity pattern (black arrow)

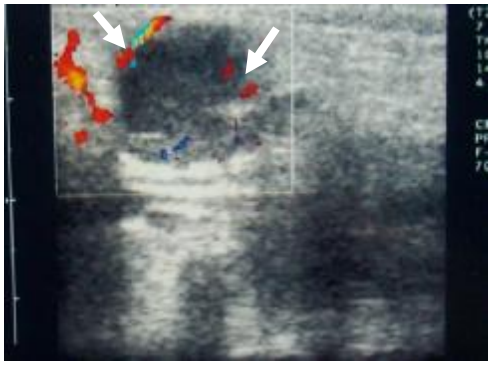

Fig (5): Color Doppler Sonography, a transverse scanning of malignant LN shows hilar with capsular vascularity pattern.(white arrow)

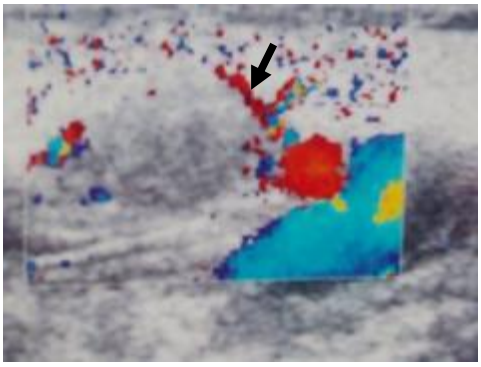

Fig (6): Color Doppler Sonography a longitudinal scanning middle cervical malignant LN shows capsular vascularity pattern initial invading internal jugular vein, internal carotid artery.

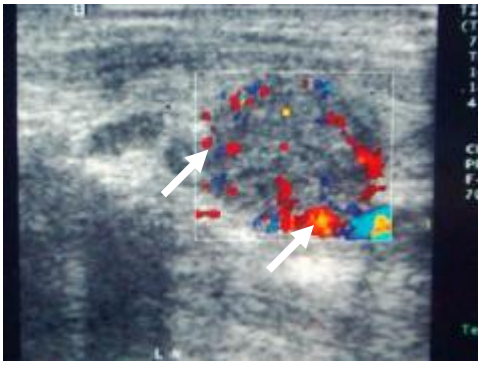

Fig (7): Color Doppler sonography: a transverse scanning of submandibular malignant LN (arrow) showing shows with hilar with capsular vascularity pattern (white arrows)