

EFFICACY OF ULTRASONOGRAPHY IN ASSESSING CERVICAL LYMPH NODE METASTASIS IN HEAD AND NECK CARCINOMA.

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Abstract

Objectives: The study was conducted to assess the value of ultrasonography (USG) for lymph node metastasis in patients with carcinoma of oral cavity. **Materials and Methods:** A total of 20 cases were selected with a primary tumor of the oral cavity. Ninety-two lymph nodes were detected by ultrasound of 5 mm or more in diameter. The patients were examined preoperatively for palpable lymph nodes clinically and ultrasonographic examination of the bilateral neck. Ultrasonographic parameters, such as size, shape, boundaries (well-delineated/ poorly delineated) and internal echoes for the lymph nodes were recorded. **Results:** The histologic positive rate was 25%, 80% and 93% for nodes between 5 and 10 mm, 10 and 15 mm and for nodes 15 mm or more in size, respectively. Ultrasonographic findings showed a high significance as the size of nodes increases. The positive rate of 86% for the round nodes of 9 mm or more in size showed a high significance. The positive rate was 93% for well-delineated nodes and 68% for poorly delineated nodes. The most frequent echo pattern was homogenous followed by hypoechoic with the positive rate for metastasis ranging from 83% to 88%. **Conclusion:** The diagnostic validity of USG as compared with histopathology showed the sensitivity of 86% and specificity of 73% with an overall efficiency of about 82% in detecting lymph node metastasis. USG is useful for preoperative evaluation of the neck, as the most reliable, inexpensive and easily available method. It is essential for diagnosis, staging, and therapy choices.

Keywords: Cervical metastasis, lymph nodes, ultrasonography

Introduction

Oral cancer is the sixth most common malignancy but in western worlds, it remains relatively rare and accounts for less than 2% of all malignant tumors; the majority are mucosal squamous cell carcinomas.^[3] There is a concern, however,

that the incidence may be increasing and oral cancer is obviously the most important tumor in the maxillofacial region. Oral squamous cell carcinoma has a relatively poor prognosis for what should be an easily diagnosed disease. It might be expected that early diagnosis would be the norm but

unfortunately, many patients still present with advanced disease.^[5] The treatment of oral cancer is also stage dependent because interference with cosmesis and function is likely to be greater in more advanced disease.^[11] It is also important to recognize that oral cancer is in some way the most challenging aspect of head and neck tumor management.^[4] Although oral cancers are included in the term "Head and neck cancer," it represents unique problems because of the critical function of the oral cavity structures. It is also more likely to require surgical intervention than other common head and neck cancers, typically laryngeal cancer, which is more often treated by radiotherapy as the sole modality.^{[2],[11]}

Invasive squamous cell carcinoma of the upper aerodigestive tract has a strong potential for metastatic spread to the cervical lymph nodes. The neck status is probably the single most important prognosticator in the head and neck cancer, as the presence of metastatic disease drastically reduces the patient's chance of survival.^[7] Clinical examination for the detection of metastasis by palpation is unreliable, as occult neck disease can occur in up to 50% of the patients, depending on the characteristics of the primary tumor.^[11] Factors that have been known to increase the risk of cervical metastasis include the site of primary tumor, tumor thickness, DNA ploidy and tumor growth patterns, such as infiltrating margins, perineural spread, and angioinvasion.^[1] Despite this knowledge, it remains difficult to accurately predict the metastatic behavior of the lesions. Many proponents of elective neck dissection find it as a diagnostic therapeutic procedure for cancers with the risk of occult metastasis of 15%-20% or higher.^[8] This, however, implies up to 80% of unnecessary operations with its associated morbidity.^[5] In addition, in a setting with shrinking resources, it has significant cost-benefit implications. The accuracy of palpation for detecting metastasis in lymph

nodes ranges between 59% and 84%, depending on the site of the primary tumor. Imaging has become the next logical step for obtaining a more accurate node stage, with the aim of more appropriate treatment. Computed tomography (CT), magnetic resonance imaging (MRI) and ultrasonography (USG) are sensitive techniques.^[12]

In general, USG is reported to be superior to palpation in detecting lymph node metastasis. Although some authors report it to be superior to contrast-enhanced CT and MRI imaging, others found similar accuracy.^[6] Advantages of USG over the other imaging techniques are its price, low patient burden and the ability of easy onscreen node measurements. Furthermore, USG is the only available imaging technique that can be used for frequent routine follow-up. Recent advances in USG concern new criteria, using high-resolution USG and power duplex Doppler, enabling the visualization of small irregularities in vascularization.^[10] However, these irregularities, probably caused by necrosis are seldom visible in lymph nodes smaller than 1 cm. USG is well suitable for follow-up after therapy.^[5] However, the repeated identical size measurements of lymph nodes do not guarantee their benign nature and these lymph nodes can suddenly start growing after many months.^[12]

Materials and Methods

The study was conducted in the oral and maxillofacial surgery department, under the topic "Detection of nodal involvement in oral cancer by ultrasound."

The aim of the study was to assess the value of USG for the investigations of lymph node metastasis in patients with carcinoma of oral cavity, as invasive squamous cell carcinoma of the aerodigestive tract has a strong potential for metastatic spread to the cervical lymph nodes. The neck status is probably the single most important prognosticator in the head and neck cancer, as the presence of metastatic disease drastically reduces the

patient's chance of survival. USG has become an established mode for the assessment of metastatic lymph nodes and particularly valuable in the examination of the soft tissue structures of the neck. A total of 20 patients (6 males and 14 females) with carcinoma of different regions of the oral cavity having clinically palpable cervical lymph nodes (suspected of metastasis) were included in this study. All the patients were examined clinically and the palpation findings of cervical lymph nodes were documented and the patients were subjected to ultrasonographic evaluation of the bilateral neck. Sixteen cases were diagnosed for squamous cell carcinoma of the primary lesion and 1 case of adenocarcinoma of the right maxillary antrum, 1 case of chondrosarcoma of right maxilla, 1 case of angiosarcoma of right mandible and 1 case of verrucous carcinoma of left buccal mucosa. 2-D Real-time B-mode ultrasonographic examinations were performed using a high-frequency (7-11 MHz) linear transducer with color Doppler. The neck was examined longitudinally and transversely using the continuous sweep technique covering the neck region bilaterally from the thoracic outlet and scalenus muscles to the submental and retroparotideal regions.

Ultrasonographic findings are documented under the following parameters:

1. Size of lymph nodes by ultrasound

2. Shape of lymph nodes by ultrasound (oval/round)
3. Boundary of lymph node (well delineated/poorly delineated)
4. Internal echoes (homogenous/hypoechoic)

These were with reference to the delineation of the adjacent vital structures, specifically internal jugular vein and the carotid artery. The findings from the clinical and USG examinations were available at the time of surgery based on which, out of the 20 cases, 2 cases underwent supraomohyoid neck dissection and 18 cases underwent radical neck dissection. The lymph nodes thus obtained surgically were examined histologically for the presence of metastasis and confirmation with the USG findings were cross checked for the true positive and true negative results. The statistical analysis was carried out using Chi-square test using SPSS software V. 8, SPSS Inc., Chicago, IL, the United States by the statistician.

Results

A total of 92 lymph nodes with a diameter of more than 5 mm were detected by ultrasound. In relation to the size of the lymph nodes [Table 2], the histologic positive rate was 25%, 80% and 93% for the nodes between 5 and 10 mm, 10 and 15 mm and for nodes of 15 mm or more, respectively. The size of the lymph nodes as determined by the ultrasonographic finding showed a high sensitivity with an increase in size.

LN size (diameter) mm	Number	Positive LN	Negative LN	Positive rate (%)
5-9	32	8	24	25
10-15	35	28	7	80
15-19	14	13	1	93
>19	11	10	1	91
Total	92	59	33	64

$\chi^2 = 33.6 (P < 0.001 \text{ HS})$

Table 2: The relationship between the histologic findings and lymph node size determined by ultrasonography

In relation to the shape of the lymph nodes as defined by ultrasound, those with a minor/major axis of more or less on ultrasound scan were considered flat (oval) and the others round. Ten of the 92 lymph nodes were flat and 9 of these were histologically negative. Eighty-two lymph nodes were round in shape [Table 3]. Among the lymph nodes ranging from 5 to 9 mm in diameter, 8 of the 25 round nodes

were positive for histology and 17 lymph nodes were negative. In the case of lymph nodes of more than 9 mm in size, 50 of the 57 round lymph nodes were positive for histopathology and 7 lymph nodes were negative. The USG findings showed a high significance for round lymph nodes of more than 9 mm in size, with a positive rate of 14% for lymph nodes of 5-9 mm and 86% for lymph nodes of more than 9 mm.

LN shape/diameter (mm)	Positive lymph nodes		Negative lymph nodes	
	Round	Oval	Round	Oval
5-9	8	0	17	7
>9	50	1	7	2
Total	58	1	24	9

$\chi^2 = 26.1 (P < 0.001 \text{ HS})$

Table 3: The relationship between the histological findings and lymph node shape determined by ultrasonography

The ultrasonographic appearance of the boundary and internal echoes of the lymph nodes were compared with histologic results [Table 4]. Sixty lymph nodes of 10 mm or more were evaluated because the characteristics of smaller nodes were difficult to analyze by USG. The boundaries

were well delineated in 41 lymph nodes with the histologic positive rate of 93% and for poorly delineated it was only 68%. The ultrasonographic findings did not show much change in the significance for lymph nodes with well delineated and poorly delineated boundaries.

HPE findings	No.	Boundary by USG	
		Well defined	Poorly defined
Negative LNs	9	3	6
Positive LNs	51	38	13
Total	60	41	19
Positive rate(%)		93%	68%

USG, ultrasonography, HPE, histopathology examination, $\chi^2 = 5.99 (P < 0.05 \text{ S})$.

Table 4: The relationship between the lymph node boundary determined by USG and histopathology findings.

The internal echoes findings were classified as homogenous and hypoechoic. Lymph nodes with homogenous echoes were completely filled with solid tumor with small amounts of fibrous stroma. The

hypoechoic lymph nodes revealed varying degrees of necrosis or fibrosis. The most frequent pattern was homogenous followed by hypoechoic pattern. The histologic positive rate was 83% and 88%,

respectively. The USG findings showed no significant change when echo pattern was considered, as the positive rate for

metastasis ranged from 83% to 88% [Table 5]

HPE findings	No.	Echo pattern	
		Homogenous	Hypoechoic
Negative LNs	9	6	3
Positive LNs	51	29	22
Total	60	35	25
Positive rate (%)		83%	88%

USG, ultrasonography. HPE, histopathology examination, $\chi^2 = 0.30$ ($P < 0.58$ NS)

Table 5: The relationship between the Echo pattern by USG and histopathology findings. Of the 92 lymph nodes detected, 5 nodes were detected in the submental region, 43 nodes in the submandibular region, 28 nodes in the upper jugular region and 16 nodes in the midjugular region. No lymph nodes were detected in the lower jugular region and posterior triangle. The positive rate ranged from 60% to 69% from submental to mid jugular region [Table 1].

LN level	No. of LNs	Positive LNs	Positive rate (%)
Level Ia	5	3	60
Level Ib	43	27	63
Level II	28	18	64
Level III	16	11	69
Total	92	59	64

USG, ultrasonography; LN, lymph node, $\chi^2 = 0.22$ ($P < 0.97$ NS).

Table 6: The relationship between lymph node levels determined by USG and histopathology findings.

Diagnostic validity of USG as compared with histopathology findings was assessed with parameters of lymph node size with the cutoff value of 9 mm, showed the sensitivity

of 86% and specificity of 73% and positive predictive value for USG of 85% and negative predictive value of 75% [Table 6].

Lymph node size (mm)	Histopathology findings		Total	
USG findings	> 9	51 ^{TP}	9 ^{FP}	60
	< 9	8 ^{FN}	24 ^{TN}	32
Total	59	33	92	

USG, ultrasonography; TP, true positive; TN, true negative; FP, false positive; FN, false negative; Sensitivity = 86%; efficiency = 82%; specificity = 73%.

Table 7: Diagnostic validity of USG findings compared with histopathology findings. The overall efficiency of USG in detecting lymph node metastasis in this study was about 82%.

Of the 20 cases, one was true negative with no metastatic lymph nodes detected on histopathology examination. Out of 92

lymph nodes detected, 51 lymph nodes of more than 9 mm in size were true positive and 9 lymph nodes were false positive. Twenty-four lymph nodes of less than 9 mm in size were true negative and 8 lymph nodes were false negative [Table 6].

Discussion

Studies have demonstrated that metastasis to the cervical lymph nodes in malignant head and neck tumors as a very important factor affecting the prognosis. Overlooking the latent lymph nodes, metastasis may result in failure of the treatment.^[3] In addition to palpation, various imaging techniques have been recommended for detection of such metastasis. An accuracy of 70% and 93%, respectively, has been demonstrated in comparison with palpation and CT of cervical lymph nodes with head and neck cancer.^[1] Importance of USG screening was shown to detect lymph nodes in a patient in whom these were not palpable.^[2] The usefulness of USG has been shown in cases of thrombosis in the jugular vein due to cervical lymph nodes, which helps in determining the association of vascular system.^{[3],[4]}

Sonography has been a useful adjunct to CT in surveying metastatic nodes when sonography and CT were compared to differentiate benign from malignant cervical lymph nodes in patients with squamous cell carcinoma of the head and neck.^[5] Sonography was shown to perform significantly better in depicting cervical metastatic nodes.^[5] Contrast-enhanced color Doppler sonography has shown a high diagnostic accuracy on the basis of vascular architecture in differentiating benign from malignant cervical lymph nodes in the head and neck tumor.^[6]

The present study compared preoperative ultrasonographic images of lymph nodes and the postoperative histopathologic diagnosis in 20 patients with carcinoma of oral cavity who underwent subsequent neck dissection and the ultrasound findings suggestive of metastasis were evaluated^[12]. The minimum

size of the lymph nodes in the neck that can be demonstrated by ultrasound is considered to be 5 mm and its usefulness compared with other methods has been reported. In this study, histopathologic positive rates were higher for larger lymph nodes, which suggested that the size is an important diagnostic criterion. This is consistent with previous studies. There was no evidence of tumor cells in lymph nodes of 8 mm or less in diameter, in a study done on 554 nodes.^[7] Positive rates of 86.5%, 93.3%, and 100%, respectively, were observed in lymph nodes with a size of 1-2 cm, 2-3cm and lymph nodes of more than 3 cm.^[8] It has been suggested that lymph nodes of 8 mm or more in size are likely to be malignant.^[4]

The change in positive rate from smaller to larger lymph nodes as determined by the ultrasonographic findings shows a high sensitivity as the size of the lymph nodes increases, with a positive rate of 25% for lymph nodes of 5-9 mm in size to 93% for lymph nodes of 15 mm and more in size. In relation to the shape of lymph nodes as defined by ultrasound, lymph nodes with a minor/major axis of more or less on ultrasound scan were regarded as flat (oval) and others round.^{[5],[8]} On USG, 10 lymph nodes were flat and 82 lymph nodes were round in shape. The negative rate for flat nodes was 78% for nodes less than 9 mm in size and 22% for lymph nodes more than 9 mm in size. The overall negative rate for flat nodes was 90% and their shape is, therefore, likely to reflect their histologic characteristics. However, the portion of lymph nodes examined was small and these were less than 9 mm in diameter. Of the lymph nodes in the range of 5-9 mm in diameter, 25 were round and 7 were oval. Eight of the round lymph nodes were positive and 17 were negative for histopathology. Of the lymph nodes more than 9 mm in size, 57 were round and 50 of them were positive and 7 were negative for histopathology. The USG findings showed a

high significance for lymph nodes round in shape when the size of lymph nodes was more than 9 mm, with a positive rate of 14% for nodes of 5-9 mm in size and 86% for nodes more than 9 mm. The accuracy of different radiologic criteria used to detect cervical lymph node metastasis showed that shape was not a valuable criterion for the radiologic assessment of the cervical lymph nodes.^[9] The shape of lymph nodes on the basis of longitudinal to transverse diameter ratio has been proposed to yield a specificity and sensitivity of 96% in sonography, 94% in MRI and 97% in contrast-enhanced CT. In lymph nodes larger than 8 mm, a ratio greater than 2 was suggested to indicate lymphadenitis with a sensitivity and specificity of 97%. Metastasis was said to show a ratio of less than 2 with a sensitivity of 87% and a specificity of 89%,^[6] whereas it was not likely with the other studies.^[5] The positive rate was 93% and 63% for well-delineated and poorly delineated lymph nodes, respectively and a well-delineated boundary is therefore highly likely to be consistent with metastasis.

Postoperatively, histologic examination suggested that the poorly defined margin in the negative lymph nodes was due to either a large amount of lymphoid cell component or a small difference in acoustic impedance between the intranodal and surrounding areas resulting from extensive fat infiltration.^[7] On the other hand, in the positive lymph nodes the margin has been clear since both internal necrosis and fibrosis with tumor cell infiltration were frequently noted in the walls of the node. Similar findings were reported in the literature.^[10]

In the present study, the boundary was well delineated in 68% (41/60) of the lymph nodes and for these, the histologic positive rate was 93%, but for the poorly delineated it was only 68%. The USG findings did not show much change in significance for lymph nodes with well-delineated and poorly delineated boundaries. Many of the

metastatic cervical lymph nodes were well delineated and the positive rate was 93%. Ultrasonographic images of the salivary glands, tongue, and floor of the mouth have been reported to be poorly defined and inhomogeneous. In a patient with esophageal and gastric cancer, USG scans revealed that all the lymph nodes surrounding the celiac axis were well delineated.^[11] In the present study, the internal echo findings were classified as homogenous and hypoechoic. The most frequent pattern was homogenous followed by hypoechoic pattern. The histologic positive rate was 83% and 88%, respectively. The USG findings showed no significant change when echo patterns were considered, as the positive rate for metastasis ranged from 83% to 88%. A study stated that nearly all examined lymph nodes were hypoechoic regardless of the histology. Reactively enlarged lymph nodes do not tend to be homogeneous and well-defined, whereas metastatic lymph nodes are frequently heterogeneous in echotexture and poorly defined. The texture of the lymph nodes and their delineation against the surrounding tissue as seen on sonography are of limited value.^[6] In this study, many of the metastatic cervical lymph nodes were well delineated and positive rates were independent of the echo pattern. Therefore, this criterion cannot be used for differentiating malignant from benign tumors in other regions.^[8] A reflective core has been reported to occur during chronic inflammation, whereas obesity and degenerative changes lead to the benign fatty replacement of lymphoid tissue. In the metastatic as with inflammatory lymph nodes, the hypoechoic rim corresponds to the lymphoid tissue.^[10] Evaluation of the association between the site and histologic findings revealed that lymph nodes in the superolateral area of the neck had the lowest positive rate. The most frequent sites of metastasis of the head and neck tumors are the submandibular and

upper jugular lymph nodes. The former are readily palpable, whereas the latter are much more difficult to find because of their location immediately below the sternocleidomastoid muscle. Therefore, the clinical value of the ultrasound in the superolateral area is noteworthy. The limitations of palpation have been demonstrated with false-positive and false-negative rates of 19.5% and 21.2%, respectively,^[12] while it was found the latter to be nearly twice as high (38%).^[13] In comparison USG was shown to be very much lower, only 5.5%.^[7] Diagnostic validity of USG as compared with histopathology findings was assessed with the parameter of lymph node size with a cutoff value of 9 mm, showed the sensitivity of 86% and specificity of 73% and positive predictive value for USG of 85% and negative predictive value of 75%. A recent study demonstrated the accuracy, sensitivity and specificity of the Vascular Index (VI) by 3-D USG, 2-D sonography, and a combination of the 2 methods for the diagnosis of metastatic cervical lymph nodes. The combination of the 2 methods yielded a higher accuracy (97% vs 85% and 89%, $P = 0.002$ and 0.016), a higher sensitivity to 2-D sonography (95% vs 81%, $P = 0.031$) and a higher specificity to VI (98% vs 75%, $P = 0.002$). The VI derived from 3D ultrasound of laryngeal cancer is a useful factor for predicting metastasis of cervical lymph nodes.^[14] Of the 20 cases [Table 6], 1 case was true negative with no metastasis detected on histologic examination. Of the 92 lymph nodes detected, 51 lymph nodes more than 9 mm in size were true positive and 9 nodes were false positive and 24 lymph nodes less than 9 mm in size were true negative and 8 lymph nodes were false negative.

Conclusion

The overall efficiency of USG in detecting lymph node metastasis in this study was about 82%. For the assessment of lymph nodes, sonographic scanning has the

advantage that it allows for free rotation of the scanning plane. The use of the ultrasonographic technique has the benefits of not using ionizing radiation, being of low cost and not being very time-consuming. USG can be used as a routine evaluation tool in the pre- and postoperative assessment of cervical lymph nodes in the head and neck cancers. USG is useful for preoperative evaluation of the neck, as the most reliable, inexpensive and easily available method. It is essential for diagnosis, staging, and therapy choices. The newer technology of 3D ultrasound can be a very useful tool for predicting metastases of cervical lymph nodes.

References

- 1) Stevens MH, Harnsberger HR, Mancuso AA, Davis RK, Johnson LP, Parkin JL. Computed Tomography of the cervical lymph nodes. Staging and management of head and neck cancer. *Arch Otolaryngol* 1988;111:735-9
- 2) Baatenburg de Jong RJ, Rongen RJ, Laméris JS, Harthoorn M, Verwoerd CD, Knecht P. Metastatic neck disease. Palpation vs ultrasound examination. *Arch Otolaryngol Head Neck Surg* 1989;115:689-90.
- 3) Bruneton JN, Balu-Maestro C, Marcy PY, Melia P, Mourou MY. Very high frequency (13 MHz) ultrasonographic examination of the normal neck: detection of normal lymph nodes and thyroid nodules. *J Ultrasound Med* 1994;13:87-90
- 4) Bruneton JN, Roux P, Caramella E, Demard F, Vallicioni J, Chauvel P. Ear, nose, and throat cancer: Ultrasound diagnosis of metastasis to cervical lymph nodes. *Radiology* 1984;152:771-3.
- 5) Sumi M, Ohki M, Nakamura T. Comparison of Sonography and CT for differentiating benign from malignant cervical lymph nodes in patients with squamous cell carcinoma of the head and neck. *AJR Am J Roentgenol* 2001;176:1019-24.

- 6) Moritz JD, Ludwig A, Oestmann JW. Contrast -Enhanced Color Doppler Sonography for evaluation of enlarged cervical lymph nodes in head and neck tumors. *AJR Am J Roentgenol* 2000;174:1279-84.
- 7) Hajek PC, Salomonowitz E, Turk R, Tscholakoff D, Kumpan W, Czembirek H. Lymph nodes of the neck: Evaluation with the US. *Radiology* 1986;158:739-42.
- 8) Snow GB, Annyas AA, van Slooten EA, Bartelink H, Hart AA. Prognostic factors in neck node metastasis. *ClinOtolaryngol* 1982;7:185-92.
- 9) Van den Brekel MW, Stel HV, Castelijns JA, Nauta JJ, van der Waal I, Valk J, *et al.* Cervical lymph node metastasis: Assessment of radiological criteria. *Radiology* 1990;177:379-84.
- 10) Marchal G, Oyen R, Verschakelen J, Gelin J, Baert AL, Stessens RC. Sonographic appearance of lymph nodes. *J Ultrasound Med* 1985;4:417-9.
- 11) Yoshinaka H, Nishi M, Kajisa T, Kuroshima K, Morifuji H. Ultrasonic detection of lymph node metastasis in the region around the celiac axis in the oesopharyngeal and gastric cancer. *J Clin Ultrasound* 1985;13:153-60.
- 12) Ali S, Tiwari RM, Snow GB. False positive and false negative neck nodes. *Head Neck Surg* 1985;8:78-82.
- 13) Martis C, Karabouta I, Lazaridis N. Incidence of lymph nodes metastasis in elective (prophylactic) neck dissection for oral carcinoma. *J Maxillofacial Surg* 1979;7:182-91.
- 14) Zhou J, Zhu SY, Liu RC, Luo F, Shu DX. Vascularity index of laryngeal cancer derived from 3-D ultrasound: A predicting factor for the in vivo assessment of cervical lymph node status. *Ultrasound Med Biol* 2009;35:1596-600.