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Radiological and Histopathological Correlation of Neck Lymph Nodes in Patients with Oral Cavity Cancers

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Abstract

Introduction: Cervical lymph nodes metastasis is a major prognostic factor in oral cavity cancers. As a result, it is critical to accurately evaluate neck lymph nodes involvement prior to treatment.

Objective: The primary goal of this study is to look into the relationship between imaging assessments (ultrasound, CT, and MRI) and histopathologic findings in order to determine the dependability of different imaging modalities in the preoperative diagnosis of neck lymph node metastases.

Methods: This retrospective study included 62 patients with oral cavity cancer who were treated in the ENT department over an 11-year period.

Results: The observed accuracy rates for ultrasound, CT, and MRI were 70%, 70%, and 74%, respectively. The observed Kappa coefficients were in good agreement (0.21,0.35,0.36 for US, CT and MRI respectively).

The discordance rate ranged between 26% and 30% and was mostly concerned with patients with radiologically underestimated lymph node status in the neck (false negative). The absence of visualization of cervical adenopathy caused radiological underestimation (false negative) of lymph node status, whereas radiological diagnostic overestimation (false positive) concerned cases where cervical adenopathy was judged to be metastatic based solely on size.

The most sensitive imaging technique was CT (53%), followed by MRI (44%), and ultrasound (33%).

The specificity rates for ultrasound, CT, and MRI were 86%, 80%, and 89%, respectively.

Conclusion: The various cervical imaging modalities evaluated in our study did not achieve satisfactory sensitivity and concordance rates, potentially leading to underestimation of lymph node status in a significant proportion of patients. As a result, we conclude that detailed histopathologic examination of pathologic staging of the lymph nodes removed during neck dissection remain the most accurate predictor of the true extent of regional metastatic spread in oral cancer.

Keywords: correlation- radiology- Histomopathology- lymph node metastasis -oral cancer

Introduction

Oral cavity cancer is the most common cancer of the upper aerodigestive tract. Squamous cell carcinoma of the oral cavity being the most predominant and associated with high morbidity and mortality. Prompt diagnosis and accurate disease staging are imperative for appropriate management [1,2].

After clinical, radiological, and endoscopic evaluations, oral cancer treatment decisions are made in a multidisciplinary consultation. [3]

Cervical lymph node invasion is an important prognostic factor for oral squamous cell carcinoma [4], so accurate imaging assessment of lymph node staging is required before surgery [5]. The main objective of our study was to evaluate the correlation between neck imaging (ultrasound, computed tomography, and magnetic resonance imaging) and definitive histological examination of cervical lymphadenopathy to determine the role of imaging in preoperative diagnosis reliability of lymph node metastasis.

Materials and Methods

We reviewed the files of 53 patients treated for oral cancer in the ENT, Head & Neck department of Ibn Rochd University Hospital over an 11-year period (September 2011-September 2021). The patients benefited from neck imaging (ultrasound Doppler, CT, MRI) prior to the tumor removal associated with a cervical lymph node dissection. The malignancy criteria considered for radiological diagnosis of lymph node metastases were: a minimum axial diameter of 10 mm, intranodal necrosis, the presence of lymph node clusters, evidence of extranodal extension. The Statistical Parameters evaluated for each imaging modality were: sensitivity, specificity, negative predictive value, positive predictive value, kappa coefficient of agreement, agreement rate (reliability), and discordance rate.

Results

-The median age of patients who underwent excision of the primary and neck dissection formed the study group is 58 years .The median time of consultation was 10 months after onset on their first symptom wish is swelling in 55%. Majority of the patients (53 %) were males.

In our study Clinical examination revealed palpable lymphadenopathy in 38,7%

(n=24), with the following characteristics: details in table 1.

Table 1: characteristics of palpable adenopathies in our patients (n24)

Laterality	Homolateral 91.7% (22 cases) Contralateral 4.2% (1 case) Bilateral 4.2% (1 case)
Percentage and number of cases by level	AI: 8.3% (2cases) BI: 33.3% (8 cases) IIA: 25% (6 cases) IIB: 4.2% (1 case) III: 4.2% (1 case) I II: 20.8% (5 cases) I II III (magma): 4.2% (1 case)
Size	Between 1 and 6 cm with an average of 2.18 cm
Mobility	Mobile in 9 cases (37.5%) Fixed in 9 cases (37.5%)
Consistency	Closed in 4 cases (16.7%) Hard in 5 cases (20.8%)
Sensitivity	Painful in 4 cases (16.7 %)
signs inflammatory	Present in 1 case (4.2%)

- No cases of synchronous head and neck tumors or extension beyond oral cavity were found.
- As part of the preoperative evaluation of the T and N stages, head and neck CT scans were performed in 66% (n=41) . 32% (n=20) benefited from a cervico-facial MRI .

Cervical ultrasound in search of lymphadenopathy was performed in 11% (n=7) alone in 4 cases and associated with cervico-facial imaging by CT or MRI in 3 patients.

In our group 5 patients were found with no cervical lymphadenopathy. In one case, necrotic adenopathy was found not vascularized on Doppler (pN+) and in the remaining case, multiple hypoechoic dedifferentiated bilateral adenopathies of centimeter size (pN0) were objectified.

-In all cases, the primary tumor removal was done with a macroscopic safety margin of at least 1 cm. *details in* table 3.

Table 3: Types of Tumor resections techniques performed

Gesture	Effective	Percentage
Tumor resection _	23	37.1%
Hemiglossectomy	16	25.8%
Partial Glossectomy	5	8.1%
Pelvi- glossectomy	6	9.7%
Trans mandibular buccopharyngectomy _	1	1.6%
Pelvi-mandibulectomy switch	1	1.6%
Hemi- mandibulectomy	6	9.7%
Subtotal Maxillectomy	2	3.2%
Hemiglossectomy + tonsillectomy + hemimandibulectomy	1	1.6%

-All our patients benefited from cervical lymph node dissection, which was unilateral in 63% (n=39) and bilateral in 37% (n=23).

The neck dissection was functional in 96% (n=82) and radical in 4% (n=4)

-The definitive histological study in our patients made it possible to identify 3 histological types: squamous cell carcinoma in 96.8% (n=60), a melanoma of the bone palate in 1 case, a mucoepidermoid carcinoma in 1 case. as shown in table 4.

Table 4: histological grade according to histological type in our study

Histological types	Histological grades	Number / Percentage
Carcinoma epidermoid n=60	Well differentiated G1 Moderately differentiated G2 infferentiated G3 N / A	42 cases /70% 10 cases /17% 6 cases /10% 2 cases /3%
Carcinoma mucoepidermoid n=1	High grade of BRANDWEIN	1 case
Melanoma n =1	N / A	N / A

In our group of study A pN+ status was found in 40,3% (n=25), The most affected level among the 38 lymph node dissections performed was sector I (14 cases), followed by level II (12 cases). Only 1 case of lymph node metastases was found in level III, 1 case for sector IV and no case for level V.

Only 1 patient (cT2N2c) with a pN+ status presented a skip-metastasis within sector III. The lymph node metastasis from level IV was associated with another from sector II. Both cases were squamous cell carcinoma of the tongue. The percentage of cases with positive nodal status on anatomic pathological examination was calculated for each clinical stage T and an increase in

this percentage was observed from T1 to T4 with a slight decrease in T3 stage. (Details in table 5)

Table 5: Distribution of patients according to cT and pN stage

STADE	pN+(cas)	pN-(cas)	% pN+/stade
T1	3	8	27%
T2	7	12	37%
T3	1	2	33%
T4	5	8	38%

In our group of study Concordance between clinical and histopathological lymph node metastasis was found in 46.8% (n=29) , while a discrepancy between the two was objectified 53.2% (n=33) : an overestimation of stage N by the clinic and/or the radiology was found in 63.6% (n=21) (33.9% of the total number of patients) while an underestimation of lymph node status was found in 36.4% (n=12) (19.4% of the total number).

Among the 32 patients classified as cN0, 28.1% were found to be carriers of lymph node metastases on anatomo-pathological examination (9 cases of occult tametastases) details in table 6

Table 6: Concordance and discordance between the clinical and histological N stages in our group of study

Stadiums	pN0	pN1	pN2a	pN2b	pN2c	pN3	Total	Concordance (%)
cN0	23	6	0	2	1	0	32	71.9%
cN1	2	1	1	0	1	0	5	20%
cN2a	0	0	0	0	0	0	0	-
cN2b	4	1	0	2	1	0	8	25%
cN2c	8	4	0	0	3	0	15	20%
cN3	0	0	0	2	0	0	2	0%
Total	37	12	1	6	6	0	62	46.8%

In our department observational reliability was 70%, 70%, and 74% for ultrasound, computed tomography, and magnetic resonance imaging, respectively.

The observed kappa coefficients were poorly consistent (0.21, 0.35, 0.36 for ultrasound, CT, and MRI, respectively). As shown in table 7

Table 7: Correlation between radiology and pathology in our study

	Kappa	Concordance (% reliability)	discrepancy	
		%	Overvaluation %	Undervaluation _ %
Ultrasound	0.21	70	10	20
CT	0.35	70	13	17
MRI	0.36	74	7	19

The discrepancy rate varied between 26% and 30%, mainly involving patients who radiographically underestimated the status of their cervical lymph nodes (false-negative results).

Radiographic underestimation of nodal status was mainly due to lack of visualization of cervical lymphadenopathy, whereas radiological diagnostic overestimation (false positive results) mainly involved

cases of lymphadenopathy Transferred based on size alone.

CT imaging proved to be the most sensitive (53%), followed by MRI (44%) and ultrasound (33%). On the other hand, the observed specificity rates for ultrasound, CT, and MRI were 86%, 80%, and 89%, respectively.

Discussion

In 2020, more than 377,000 new cases of oral cavity cancer (C00-C06 of the ICD-10) were recorded worldwide and more than 177,000 deaths are to be deplored from the consequences of this disease according to GLOBOCAN estimates.

Oral cavity cancer is the most common cancer of the upper aerodigestive tract. It ranks 8th among cancers in order of frequency in men, 15th in women and 18th in both sexes combined among 36 other cancer sites [6-7].

The incidence and mortality rates of these cancers are increasing over the years, especially in middle and low income countries. This may be due to the fact that developed countries have more manpower and financial resources to invest in basic oral health care, which increases the rate of early detection of oral cavity cancer and improves the prognosis of this disease. On the other hand, patients with oral cavity cancer need a complex, always multidisciplinary approach including surgery, radiotherapy, chemotherapy, targeted therapy and other therapies, which is easier to implement. implemented in developed countries [8,9].

Ultrasound is one of the most commonly used imaging techniques and represents a very valuable diagnostic tool for the staging and follow-up of cancers. Its advantages are its wide availability, its economic cost, the absence of radiation exposure and in general, no contrast medium is necessary.

On the other hand, the disadvantage of this technique lies in the fact that it is incapable of exploring deep structures (depth greater than 3-4 cm). Furthermore, it is operator-dependent unlike other cross-sectional imaging modalities [10-11].

In our series, the sensitivity of ultrasound proved to be unsatisfactory with a rate of only 33% against a specificity of 86%, which implies that its role was limited in the detection of lymph node metastases in our patients.

Our results were comparable to those of certain authors, Qiao,Y et al.[12] objectified rates sensitivity and specificity of 30.8% and 70.2% respectively.

In the others series [11-13-14-15], the rates varied between 54% and 90.5% for sensitivity, between 79.4% and 99.4% for specificity, between 57.6% and 92.3% for predictive value positive and between 77.1% and 98.2% for the negative predictive value, the values most elevated were mainly observed when the study was prospective [13-14-15.]

The reliability of the ultrasound examination differed between the series, Qiao, Y et al.[12] found a rate of only 45.6% against 76% in the series Shetty, D et al.[17], the rate of reliability in our study was 70%, a percentage that was comparable to those of CT and MRI. However, good significance was not achieved.

On the other hand, computed tomography and MRI are considered imaging techniques that offer the possibility of evaluating both superficial and deep structures, although the resolution is limited to approximately 3 mm depending on the protocol used. MRI would be preferred to CT in cases where excellent soft tissue contrast is required, the opposite if extension to bone is to be assessed. Contrast products standard iodines used carry a risk in patients with renal insufficiency as well as a risk of interfering with the functions of the thyroid gland, whereas the Gadolinium commonly used for MRI is

generally well tolerated. Allergies to iodinated contrast media are far more common than adverse effects of gadolinium[11].

In our series, we have objectified sensitivity rates of 53%, 44% and specificity rates of 80% and 89% for CT and MRI respectively.

Rates similar to those in our study have been observed in the literature, Woolgar , J et al[13] found a sensitivity of 49%, Bergman, SA et al[16] and Mazzawi , E et al.[18] found objectified sensitivity rates of 55% and 48% respectively with regard to CT imaging . On the other hand, a rate of 31.8% was observed in the series Shetty D et al.[17] against a specificity of 93.8% knowing that this prospective study took into account the same criteria of malignancy on which we based ourselves in our series.

Regarding the sensitivity of magnetic resonance imaging, results comparable to ours were noted in the series of Mazzawi , E et al. [18], with a rate of only 43% against a specificity of 70%.

In the series [11-18-19], the sensitivity of the computed tomography was well

superior to that of MRI, which was the case for our study. However, according to other studies [20-21], the opposite has been observed.

The precision of imaging concerning the diagnosis of lymph node metastases (the concordance rate between imaging and pathological examination) was 70% for CT and 74% for MRI in our series.

In the literature [12-15-13-17], the reliability of computed tomography varied according to the studies between 42.2% and 96.1% while the concordance rates (reliability) concerning MRI found in the literature [22 -23,] were higher than those objectified in our study. According to Thomsen JB.[22], rates of 36%, 93%, 85% for sensitivity, specificity and reliability respectively, were observed . On the other hand, Ding Z- X.[23] found a concordance rate of 86.4% with a sensitivity of 79.5%, however this study considered a threshold of minimum size which corresponds to 8mm against that of 10 mm taken into account in our series.

In most series [12-13-14-15-16-17-18] including ours, imaging (ultrasound, CT, MRI) showed good specificity compared to its sensitivity. This can be explained by several hypotheses.

In imaging, a significant discrepancy concerning the proposed size threshold has been observed in the literature, no threshold has shown excellent specificity with good sensitivity with regard to the ability to differentiate between metastatic adenopathy and another reactive one. According to the study by Curtin , HD et al.[19], when height is the only criterion taken into account to define the cN status of a patient, better sensitivity was achieved in CT and MRI with a threshold of 5 mm at the cost of poor specificity, while the best specificity was achieved with a threshold of 15mm . When size is associated with other malignancy criteria, in particular signal or density abnormalities, the sensitivity rate improved from the threshold of 9 mm. This leads to the conclusion that on the one hand, for good sensitivity, a lower size threshold must be considered and on the other hand, the size alone is not reliable enough to determine the nature of a lymph node. However, if the lymph node is small, it would be difficult to assess the other criteria of malignancy on imaging. According to King, A and al.[24] no imaging modality made it possible to assess the character of necrosis within the lymph nodes whose diameter is less than 3 mm.

In our series, the major criteria of malignancy that have proven to be reliable (true positives) in imaging are the presence of a cluster of adenopathies (100% true

positives, 2+/2 cases) and intra-nodal necrosis (85.7% true positives, 6+/7 cases), a diameter ≥ 10mm alone has currently only proven to be reliable in 43.8%.

On the other hand, among the 10 cases of false positives collected in our series, 9 cases or 90% were considered positive according to the size criterion only (≥ 10 mm). Some authors have stated that the two main pitfalls in the radiological evaluation of lymph node metastases are: the difficulty of determining whether an enlarged lymph node is metastatic or the site of reactive adenitis, and the inability to detect metastatic disease in lymph nodes that are not "normal" size necroses[25].

Based on a meta-analysis [20], sensitivity and specificity results were grouped according to study type. It turned out that for the studies carried out retrospectively, the average rate of sensitivity was lower than that of the prospective studies: the diversification of the protocols used in imaging and the interpretation of radiological images by various specialists may explain this relatively low rate.

An unsatisfactory sensitivity rate implies that there is a non-negligible rate of false negatives. In our series, an underestimation of lymph node status in radiology was found in 16 cases, it was mainly due to the absence of visualization lymphadenopathy in 62.5%. Two possible hypotheses are to be put forward: on the one hand, the frequency of occult lymph node metastases in cancers of the oral cavity can explain these false negatives and on the other hand, a relatively long delay between the realization of the initial radiological assessment and the surgical treatment could be responsible on the one hand for the discrepancies observed between the radiology and the anatomopathological examination in these cases.

Among patients with oral cavity cancer with clinical and radiological status N0, 20–30% have occult lymph node metastases [26–27]. In our series, 28.1% of patients classified as cN0 currently had lymph node metastases (pN +). No imaging method can reliably detect microscopic metastatic foci within lymph nodes.

immuno -histochemical and molecular analysis techniques are more sensitive compared to examination under an optical microscope with hematoxylin staining and eosin [28].

In our study, the average delay between the radiological assessment and the diagnosis pathology was 45 days with extremes of 2 days and 8 months.

Some authors [28-30] have objectified a significant association between a relatively long treatment time and a poor prognosis as well as an advanced stage on histological examination in cancers of the oral cavity.

Tableau XXV : Comparaison entre les taux de sensibilité, spécificité et fiabilité(concordance) de l'imagerie dans la littérature.

		Echographie			TDM			IRM		
ETUDE	TYPE	Se	Sp	F	Se	Sp	F	Se	Sp	F
Woolgar, J A et al.(73)	R				49%	87%	73%			
Bergman, S A et al(74)	P				55%	90%				
Mazzawi, E et al(121)	R				48%	76,3%		43%	70%	
Shetty, D et al(75)	P	54%	85%	76%	31,8%	93,8%	76%			
Jhony, K et al(119)	P	90,5%	90,9%	31,6%						
Mishra, N et al.(120)	P	80%	99,4%	97,7%	86%	97%	96,1 %			
Qiao, Y et al(118)	R	30,8%	70,2%	45,6%	33%	68,6%	42,2 %			
Sun, J et al(123)	R				52%-80%	68%-81%		70%-81%	72%-80%	
El Kininy, Wet al(124)	P				63%			74%		
Laimer, J et al(117)	R	54,3%	79,4%		95%	63,9%		85,7%	75,6%	
Thomsen JB.(125)	P	87%	85%	85%				36%	93%	85%
Ding Z-X.(126)	R							79,5%	90,4%	86,4 %
Notre étude	**R**	**33%**	**86%**	**70%**	**53%**	**80%**	**70%**	**44%**	**89%**	**74%**

Conclusion

The patient's lymph node status plays a major role in the prognosis of oral cavity cancers, hence the need for an adequate clinical and paraclinical preoperative evaluation in order to detect a possible regional metastatic disease.

Nevertheless, the different cervical imaging modalities evaluated in our study (ultrasound, computed tomography, magnetic resonance imaging) did not show satisfactory sensitivity and could lead to underestimations of lymph node status in a significant proportion of patients.

The rate of discrepancy observed mainly concerned cases in which a radiological under-evaluation of the lymph node stage was highlighted, this calls into question the reliability of the various criteria of malignancy used in imaging, in particular, the size criterion.

For better preoperative determination of lymph node status, other techniques may prove to be more reliable, in particular the sentinel lymph node technique and hybrid imaging. Until the introduction of new terms and conditions imaging, surgical treatment by cervical lymph node dissection in patients with cancers of the oral cavity remains the best choice in our context.

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