Original Article

What is the consistency between clinical and pathological staging in tongue cancer?

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ABSTRACT

Objectives: This study aimed to evaluate the consistency between clinical and pathological staging in tongue cancer.

Patients and Methods: We retrospectively evaluated 33 patients (24 male, 9 female; mean age 56±13 years; range, 31-87 years) who were admitted to the Şişli Hamidiye Etfal Training and Research Hospital Otorhinolaryngology Head and Neck Surgery Clinic and operated on for tongue cancer. The clinical stages were determined with physical examination and radiological findings. The consistency of the clinical stages with pathological stages was evaluated with Mc Nemar Analysis and Kappa test.

Results: For tumor (T) stage, the clinical and pathological stage estimate was 60.6% compatible whereas for cervical lymph node (N) stage it was 54.5%. There was poor agreement between clinical and pathological stages.

Conclusion: In order to make more accurate clinical staging and to overcome poor agreement between clinical and pathological staging, more detailed and additional radiological imaging with a comprehensive physical examination are required. Routine preoperative positron emission tomography scanning and radiological examination of the tumor by an expert head and neck radiologist and evaluation by a pathologist experienced in head and neck malignancies is recommended.

Keywords: Cancer staging; neck dissection; prognosis; tongue cancer.

Tongue cancers comprise 5% of all body cancers and almost half of oral cavity cancers.[1] Determining the stage is as important as making the diagnosis of cancer. Staging provides a common language and also is required in order to choose the proper treatment plan, have an opinion about prognosis and compare results with the literature. Physical examination and conventional imaging methods are classically used for determining the extension of the tumor and nodal metastasis.

The tumor node metastasis (TNM) staging system was developed and maintained by the American Joint Committee on Cancer Staging (AJCCS) and the Union for International Cancer Control. The TNM classification defined by the AJCCS is the most commonly used staging

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system for tongue cancer around the world. This staging system is based on the size and the local invasion of the primary tumor (T), size and number of cervical lymph nodes (N) and the presence of distant metastasis (M).[2,3]

Differences between clinical and pathological staging of tongue cancer are known.[2] This study aimed to compare clinical staging of tongue with pathological staging in our clinic and evaluate the consistency between them.

PATIENTS AND METHODS

We retrospectively evaluated 33 patients (24 male, 9 female; mean age 56±13 years; range, 31-87 years) who were admitted to our otorhinolaryngology head and neck surgery clinic in a tertiary care hospital due to tongue cancer and who underwent surgery between April 2007 and May 2017. Patients with other head and neck cancers, missing preoperative computed tomography (CT) or magnetic resonance imaging (MRI) or histopathological results, and patients who were treated non-surgically were excluded from the study.

The study was approved by the Şişli Hamidiye Etfal Training and Research Hospital Ethics Committee (Approval number: 23.12.2014/813).

Clinical and radiological data of the patients who had been operated on due to tongue cancer were obtained from the clinical and hospital medical records. Physical examination findings, routine laboratory tests and radiological imaging results were noted. For oncological cases such as tongue cancer, routine detailed examination

Table 1. Demographic distribution of the patients and their clinical and pathological tumor (T) and cervical lymph node (N) stages

	n	%	Mean±SD	Range
Age (year)			56.3±13.2	31-87
Gender				
Male	24	72.7		
Female	9	27.3		
T clinical stage				
T_1	14	42.4		
T_2	12	36.4		
T_3	7	21.2		
T pathological stage				
T_1	14	42.4		
T_2	14	42.4		
T_3	5	15.2		
N clinical stage				
N_0	17	51.5		
N_1	9	27.3		
N_{2a}	1	3.0		
N_{2b}	3	9.1		
N_{2c}	3	9.1		
N pathological stage				
N_0	15	45.5		
N_1	6	18.2		
N_{2a}	1	3.0		
N_{2b}	8	24.2		
N_{2c}	3	9.1		

T: Tumor; N: Node; SD: Standard deviation.

Table 2. Surgical methods and the levels of the neck dissection applied to the tongue cancer patients

	n	%
Surgical method		
Partial glossectomy	20	60.6
Hemiglossectomy	11	33.4
Subtotal glossectomy	2	6
Type and level of the neck dissection		
Ipsilateral level 1, 2, 3 neck dissection	18	
Ipsilateral level 1, 2, 3, 4 neck dissection	6	
Bilateral level 1, 2, 3, 4 neck dissection	4	
Ipsilateral level 1, 2, 3, 4 and contralateral level 1, 2, 3 neck dissection	4	
Ipsilateral level 1, 2, 3, 4, 5 and contralateral level 1, 2, 3, 4 neck dissection	1	

findings had been done under supervision of a senior surgeon and control examinations done by senior surgeons had also been noted in the medical records and data was obtained from these. All patients had been examined in detail for primary tumor and cervical metastasis. Routine laboratory tests and chest X-rays had been performed on all patients. For all tongue cancer patients, MRI with 1.5 Tesla MRI device (Philips Intera Achieva; Philips Medical Systems, Nederland) had been preferred for preoperative staging of the tumor and neck unless contraindicated for the patient. In case of suspicion of bony invasion, CT images with 3 mm interslice distances had been obtained using a Somatom Plus 4 CT scanner (Siemens AG, Erlangen, Germany). All of the imaging scans were re-evaluated by the same radiology specialist in order to achieve standardization.

Clinical TNM staging of the tongue cancer had been determined after physical examination and radiological findings according to the AJCC.

The patients had been treated with tumor resection and defect reconstruction and ipsilateral or bilateral neck dissection surgically. The type and extent of neck dissection had been decided according to clinical staging and location of the tumor (midline or lateral).

Surgical specimens had been examined histopathologically by senior pathologists after fixation in 10% formalin. Tissue blocks obtained from the specimens had been embedded in paraffin and stained with hematoxylin-eosin (HE) after 5 micron sections in three planes had been obtained. The slides had been examined under light microscopy. Size, vascular or perineural invasion, differentiation and surgical borders of the tumor, bony invasion, number of metastatic cervical lymph nodes or extracapsular invasion had been mentioned in the histopathological reports of the patients. The pathological staging of patients had been established according to these findings.

Table 3. Comparison of the concordance between the clinical and pathological T stage

	T_1	T_2	T_3	Total
T_1				
Number	9	5	0	14
Line percent	64.3	35.7	0.0	100
Column percent	64.3	35.7	0.0	42.4
T_2				
Number	4	7	1	12
Line percent	33.3	58.3	8.3	100
Column percent	28.6	50.0	20.0	36.4
T_3				
Number	1	2	4	7
Line percent	14.3	28.6	57.1	100
Column percent	7.1	14.3	80.0	21.2
Total				
Number	14	14	5	33
Line percent	42.4	42.4	15.2	100
Column percent	100	100	100	100

McNemar-Bowker test p=0.695; Kappa: 0.378.

Clinical stages of the patients were noted from the documents and then compared with pathological stages and concordance between them was evaluated.

Statistical analysis

Statistical analysis was performed with SPSS for Windows version 15.0 software (SPSS Inc., Chicago, IL, USA). The numerical variables were expressed in mean, standard deviation (SD), minimum and maximum values. Categorical variables for descriptive statistics were expressed in number and percentage. The comparison of dependent groups was performed with McNemar analysis and Kappa test was used for consistency analysis. Statistical significance was defined as $p<0.05$.

RESULTS

Demographic data with clinical and pathological staging of the patients are listed in Table 1. Thirty-three patients had been operated on due to tongue malignancy. Partial glossectomy was performed in 20 patients, hemiglossectomy in 11 patients, and subtotal glossectomy in two patients. Ipsilateral level 1-3 neck dissections had been performed in 18 patients and ipsilateral level 1-4 neck dissection in six patents. In nine patients in whom the tumor approximated or crossed the midline, bilateral neck dissection had been performed. Bilateral level 1-4 neck dissections in four patients, ipsilateral level 1-4 and contralateral level 1-3 neck dissections in four

Table 4. Comparison of the concordance between the clinical and pathological N stage

N clinical stage	N_0	N_1	N_{2a}	N_{2b}	N_{2c}	Total
N_0						
Number	13	1	0	2	1	17
Line percent	76.5	5.9	0.0	11.8	5.9	100
Column percent	86.7	16.7	0.0	25.0	33.3	51.5
N_1						
Number	1	3	1	2	2	9
Line percent	11.1	33.3	11.1	22.2	22.2	100
Column percent	6.7	50.0	100	25.0	66.7	27.3
N_{2a}						
Number	0	0	0	1	0	1
Line percent	0.0	0.0	0.0	100	0.0	100
Column percent	0.0	0.0	0.0	12.5	0.0	3.0
N_{2b}						
Number	0	1	0	2	0	3
Line percent	0.0	33.3	0.0	66.7	0.0	100
Column percent	0.0	16.7	0.0	25.0	0.0	9.1
N_{2c}						
Number	1	1	0	1	0	3
Line percent	33.3	33.3	0.0	33.3	0.0	100
Column percent	6.7	16.7	0.0	12.5	0.0	9.1
Total						
Number	15	6	1	8	3	33
Line percent	45.5	18.2	3.0	24.2	9.1	100
Column percent	100	100	100	100	100	100

McNemar-Bowker test p=0.685; Kappa: 0.336.

Table 5. Clinical T and N stages and comparison with the pathological stage of tongue cancer patients

Clinical stage	n	%
T stage		
Correct stage	20	60.6
Over stage	7	21.2
Under stage	6	18.2
N stage		
Correct stage	18	54.6
Over stage	5	15.1
Under stage	10	30.3

patients, ipsilateral levels 1-5 and contralateral levels 1-4 neck dissections in one patient (Table 2). Patients with neck metastasis and/or extracapsular invasion had been treated with adjuvant radiotherapy or radiochemotherapy decided according to our hospital tumor council.

Clinical T staging was 60.6% compatible with the pathological T staging. There was poor agreement between clinical T staging and pathological T staging (Kappa: 0.378) (Table 3). Clinical N staging also showed poor agreement with pathological N staging. The clinical N staging was 54.5% compatible with pathological N staging (Kappa: 0.336) (Table 4).

Clinical T staging was reported to be correct in 20 (60.6%), overestimated in seven (21.2%) and underestimated in six patients (18.2%). Clinical N staging was observed to be correct in 18 (54.6%), overestimated in five (15.1%) and underestimated in 10 patients (30.3%) (Table 5).

DISCUSSION

Staging is one of the major factors that lead to an accurate treatment plan and prediction of prognosis in patients with tongue cancer. The AJCC TNM classification system is preferred by many clinicians for tongue cancer staging. Physical examination and imaging methods are required for staging and treatment planning. Improvement of the staging system is important for better patient stratification. For this purpose, the AJCC published the 8th edition of the cancer staging manual in 2016 in which two new parameters (depth of invasion and extranodal extension) were included.[2,3] Radiological evaluation could give an idea of depth of the tumor invasion and extranodal extension preoperatively. However, more accurate results are obtained after pathological examination. In the present study the pathological specimens were not re-evaluated so staging of the tongue tumors was performed according to the AJCC staging system that was published in 2010.

In this study clinical T staging was reported as correct in 20 (60.6%), higher in seven (21.2%) and lower in six patients (18.2%). We underestimated five patients as T_1 stage while they were T_2 and one patient was underestimated as T_2 while the correct stage was T_3. This could be due to wrong estimation of tumor depth and induration, as physical findings only assessed the outside of the lesion. Imaging methods also seemed to be less helpful in this assessment.

In order to overcome under- or over-treatment, we recommend frozen sections from the surgical area and a detailed re-examination of the tumor under general anesthesia with the help of muscle relaxants which may provide a more accurate estimation of the size of the tongue tumor. In our clinic, perioperative specimens from the surgical margins were sent to the pathology department and frozen sections were evaluated. Surgical margins were confirmed by frozen sections in all of the patients with tongue tumors. If there was suspicion of close margins, then surgery was extended until healthy margins were reached.

On the other hand seven patients were overestimated for T stages. Five patients with T_1 stage were evaluated as T_2 and two patients with T_2 stage were staged as T_3 preoperatively. Hemiglossectomies were planned for these patients. Although the T stages were over estimated, since surgical margins were perioperatively estimated, extra tongue tissue was not removed.

The most important prognostic factor in head and neck cancers is the condition of cervical lymph nodes. This is also valid for tongue cancers. Presence of a single lymph node reduces survival approximately 50%. So the correct treatment of cervical lymph nodes is critically important for the patient.[4-6] Tumor invasion depth is also effective in prognosis.[7,8]

It should be kept in mind that the experience of the physician is important for cervical lymph node evaluation and thus it is partially subjective. Generally convenient types of neck dissection can be performed depending on the primary tumor and the lymph node(s) of patients in whom suspicious lymph node(s) are detected on physical examination.[9] In the present study clinical N staging done by physical examination and radiological evaluation revealed that N staging was detected as correct in 18 (54.6%), higher in five (15.1%) and lower in 10 patients (30.3%) in clinical staging. The clinical N staging was 54.5% compatible with the pathological N staging (Kappa: 0.336).

In terms of N stages the clinical staging were not very accurate. Estimated N stages in 10 patients were lower than the correct stages which was especially important. Preoperative positron emission tomography (PET) imaging and fine needle aspiration biopsy of lymph nodes can provide additional information about the neck metastasis.[10,11]

Determining the relationship between the anatomical structure and the function of the tongue is of importance for surgical planning and quality of treatment. Also there are micrometastases that cannot be detected with conventional imaging methods in 20-30% of early stage T_{1-2}, N_0 tongue cancers.[12] Besides, the location of the tongue within the oral cavity makes its evaluation difficult. Preoperative detection of tumors which have a risk for occult metastases may increase survival rates by preventing unnecessary over treatment and emergence of late metastases. Magnetic resonance imaging is a common imaging modality for the analysis of structural and functional analysis of the tongue and neck metastasis.[13-15] Navarro et al.[14] have shown that MRI is a useful imaging method for preoperative evaluation of tongue cancers and tumor thickness.

In the present study we also used MRI for the radiological evaluation of the tumor and lymphatic metastasis preoperatively and CT imaging in cases with suspicion of bony invasion.

Lately depth of invasion was added to 8th edition AJCC on cancer guidelines for T staging of HPV negative oral cavity squamous cell carcinoma.[3] The need for prophylactic neck dissection in patients with N_0 tongue cancer is often based on the tumor size in addition to the radiographic assessment of depth of the invasion.[16] We consider that a more correct preoperative T staging and a more detailed invasion depth evaluation would be beneficial for determining prognosis and treatment plan and perhaps this may change our staging system.

All these findings make accurate preoperative staging important. Treatment and prognosis is determined by evaluating clinical and radiological staging together. Insufficiency in staging, the conditions which limit the correct evaluation of imaging methods and proper physical examination continue to be a problem today.

In our clinic, preoperative physical examinations of patients was done by different residents under the supervision of senior surgeons. Perhaps physical examination of patients under general anesthesia should again be done during surgery and noted in their medical record. For the those in whom the stages were inconsistent, the reasons could be discussed case by case.

In this study, while collecting the radiological data from the medical notes the radiological reports had been evaluated and written by different radiologists. Routine PET scanning which could have helped in determining neck and distant metastasis was not applied in all of the cases. In order to achieve standardization, the same radiologist re-evaluated the radiological findings of the patients for this study. For making the most accurate tumor stage and evaluation, an expert radiologist for head and neck malignancies should be determined by the oncological team for routine evaluation.

Also for pathological examination, perioperative cooperation should be achieved. In case of need, one of the members of the surgical team and a pathologist should examine the specimen together for anatomical domination. Preoperative frozen section evaluation is also important for planning treatment. This can help in reducing inconsistency and determining the surgical margins and neck metastasis.

Standardization of the physical examination, radiological evaluation and pathological examination are the key points for determining the most correct tumor stage and decreasing inconsistency. For all of the oncological cases including tongue cancer patients, preoperative evaluation of physical and radiological findings should be discussed by the oncological team including the surgeon, radiologist, pathologist, medical oncologist, radiation oncologist and nuclear medicine specialist. After pathological examination, if there is inconsistency of the stages, the case should be re-evaluated and the reasons for the inconsistency should be determined.

There are some limitations in this study. The sample size of the study is small. Only patients operated on for tongue cancer and those with preoperative imaging scans were included in the study. Studies with larger cohorts may provide additional insight concerning the preoperative tumor staging and the outcomes. This is also a retrospective cohort study and it may be speculated that there could be some limitations including bias and availability of information in the medical notes from which parameters were taken into consideration. In our ENT department, there is an established database program which contains medical information, physical examination and radiological findings concerning oncology operations. Medical notes were taken from patients and otorhinolaryngological examination was done by different residents under the supervision of senior surgeons. By this means, we tried to keep prejudiced information to a minimum.

In our study, clinical and pathological staging of tongue cancers were found to be poorly consistent for T and N staging. The medical team should be aware of the possibility of this poor consistency. In order to overcome this problem, proper physical examination done by all of the members of surgical team under supervision of a senior surgeon and more detailed radiological examination with additional imaging methods like PET scanning are recommended. For the standardization of radiological and pathological evaluation, maybe it can be further recommended that only a radiologist experienced in head and neck should evaluate the imaging of this region and only a pathologist experienced in head and neck malignancies should examine the specimens.

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