Comparison of Clinical and Pathological Staging in Patients with Head and Neck Cancer After Neck Dissection

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Int Arch Otorhinolaryngol 2023;27(4):e571–e578.

Abstract

Introduction Clinical and pathological staging plays an important role on the prognosis of head and neck cancer (HNC) patients.

Objective The present study aims to compare clinical and pathological T, N and overall staging in patients with HNC, to identify factors associated with these discrepancies, and to analyze and compare survival or disease-free survival in staging disagreements.

Methods Retrospective cohort including every patient submitted to neck dissection from January 2010 to December 2020 in the department of Otorhinolaryngology of a tertiary hospital center.

Results A total of 79 patients were analyzed; their mean age was 58.52 ± 13.15 years old and 88.9% were male. Assessing overall staging, discrepancies were noted in 53% (36.4% upstaging and 16.6% downstaging) and were significantly associated with clinical overall staging ($p = 0.006$). Regarding T staging, differences were noted in 45.5% (30.3% upstaging and 15.2% downstaging) and were significantly associated with imaging modality ($p = 0.016$), clinical T staging ($p = 0.049$), and histology ($p = 0.017$). Discrepancies in N staging were noted in 38% (25.3% upstaging and 12.7% downstaging) and were significantly associated with age ($p = 0.013$), clinical N staging ($p < 0.001$), and presence of extranodal invasion ($p < 0.001$). Both in Overall, T, and N staging, the aforementioned disagreements were not associated with either higher mortality or higher disease relapse.

Conclusion Overall, T, and N staging disagree in an important number of cases, and the overall stage can disagree in up to 53% of the cases. These disagreements do not seem to influence overall and disease-free survival.

Keywords
- head and neck cancer
- neck dissection
- squamous cell carcinoma of head and neck

received
November 14, 2021
accepted after revision
June 30, 2022
article published online
September 14, 2023

DOI https://doi.org/10.1055/s-0042-1758208.
ISSN 1809-9777.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Introduction

Head and neck cancer (HNC) comprises the seventh most common cancer worldwide[1] and its most common histological type is squamous cell carcinoma.[2] Five-year survival in HNC has improved since 1990, from 54.7% in 1992 to1996 to 65.9% in 2002 to 2006, in part due to advances in treatment options and the improvement in survival conferred by Human papillomavirus (HPV)-positive tumors.[3] The prognosis of HNC is determined mainly by anatomic site, stage, and HPV status with a role for other pathologic and clinical factors, such as extranodal disease, positive surgical margins, perineural invasion, age, comorbidities, and tobacco use, among others.[4] Staging must be performed before treatment (clinical staging) and after surgical resection (pathologic staging). Clinical staging (cTNM) results in a combination of clinical examination, endoscopy and imaging by computed tomography (CT), magnetic resonance imaging (MRI), ultrasound or positron emission tomography/computed tomography (PET-CT), either isolated or combined.[5] On the other hand, for pathological staging (pTNM), surgical removal of tissue and a detailed histopathological analysis are necessary.[6] Disparities between both clinical and pathological staging methods in HNC have been found and reported in the literature by many authors.[7–15] A study with 501 patients with HNC found discrepancies between clinical and pathological staging in at least 1 staging category to be present in almost 50% of the cases. In addition to this, they found that even though both clinical and pathologic staging methods seem to be useful in predicting survival, pathological nodal category seems to be the strongest predictor.[9] Since an accurate clinical staging is paramount for patient counselling, treatment planning, prognosis or to design clinical trials,[14] it is important to be aware of the potential extent of disparity that may exist between both methods.

In the present study, we assessed and compared clinical and pathological Overall, T and N staging data in patients who underwent neck dissection (ND) from 2010 to 2020. The primary objective was to calculate the rate of disparities and analyze factors that could be associated with these differences in staging. Furthermore, we evaluated five-year overall survival and disease-free survival between patients with either identical, downstaging or upstaging pathological findings.

Methods

Observational retrospective longitudinal study including every patient with HNC submitted to ND with or without primary tumor resection from the 1st of January 2010 to the 31st of December 2020 at the department of otorhinolaryngology from a tertiary hospital center. Patients without the necessary clinical or pathological staging data were excluded.

Data collection was performed in March 2021. Demographic and clinical data were collected by analyzing the medical records of the patients. Tumor staging was in accordance with the 8th edition of the American Joint Committee on Cancer (AJCC).[6] Clinical staging was collected by interpreting the reports of preoperative imaging exams, which could be either CT, MRI, both, or PET-CT and pathological staging, was collected by interpretation of histopathological reports. The clinical stage of patients with relapsing disease was collected in the imagological exams closest to the date of surgery. Follow-up data from patients who were alive without disease relapse was registered as censored at the last follow-up contact.

A descriptive analysis of the characteristics of the patients was performed, taking into consideration absolute and relative frequencies for categorical variables, mean and standard deviation (SD) for normally distributed continuous variables, and median and range for non-normally distributed continuous variables. Clinical and pathological T, N, and overall stages were compared by crosstabulation and the patients were categorized as having an identical, upstaging, or downstaging pathological stage. The Cohen Kappa coefficient was estimated to assess agreement between both staging methods and was interpreted according to Landis et al.[16] Comparisons between groups were made with the chi-squared test or with the Fischer exact test for categorical variables, with the Student *t*-test for normally distributed continuous variables, and with the Mann-Whitney U-test for non-normally distributed continuous variables. The normality of continuous variables was assessed with the Kolmogorov-Smirnov test. Only univariate analysis was performed since the sample number wasn't large enough for a multivariate analysis. Survival curves were made with the Kaplan-Meier method and differences were examined with the log-rank test. All statistical analyses were made with IBM SPSS Statistics for Windows version 27 (IBM Corp., Armonk, NY, USA) and associations were considered significant when $p < 0.05$.

Ethical approval was obtained from the Hospital Ethics Committee with the number 27/2022.

Results

A total of 85 NDs were performed from January 2010 to December 2020. After exclusion of patients without complete clinical and pathological data, there was a total of 79 NDs for analysis. The basic characteristics of the patients submitted to surgery are listed in ►**Table 1**. The mean age of the patients was 58.52 ± 13.15 years old and 88.9% of the patients were male. Overall staging prior to surgery was I/II in 39.3% of the cases and III/IV in 60.7%; 16.5% of the NDs were performed for relapsing disease following previous surgery or treatment with chemotherapy and/or radiotherapy, and 7.6% of the surgeries were a revision ND.

For N staging analysis, all the 79 patients were included. When comparing overall and T clinical and pathological stagings, cT0 patients were excluded, resulting in the inclusion of only 66 patients in these two analyses. Clinical T0 corresponded to patients with nodal relapsing disease or nodal metastasis of unknown primary.

Overall Staging Analysis

Regarding overall staging, agreement between clinical and pathological stages was fair (Cohen Kappa: 0.291; $p < 0.001$), and differences were noted in 53% of the surgeries, of which

Table 1 Characteristics of the patients

Age (mean ± SD)		58.52 ± 13.15
Female		8 (10.1%)
Primary tumor site	Pharyngeal	13 (16.5%)
	Oral cavity	26 (32.9%)
	Laryngeal	28 (35.4%)
	Others	12 (15.3%)
Hystology	Squamous cell carcinoma	72 (91.1%)
	Others	7 (8.9%)
Side	Right	45 (57%)
	Left	25 (31.6%)
	Midline/bilateral	9 (11.4%)
Previous ND		6 (7.6%)
Recurrent disease		13 (16.5%)
Overall stage	I	19 (24.1%)
	II	12 (15.2%)
	III	15 (19%)
	IVa	32 (40.5%)
	IVb	1 (1.3%)
END side	Bilateral	58 (73.4%)
	Right	14 (73.4%)
	Left	7 (8.9%)
Tobacco consumption		49 (62.03%)
Alcohol consumption		21 (26.58%)

Abbreviations: END, elective neck dissection; SD, standard deviation.

36.4% had a higher and 16.6% a lower pathological stage when compared with the overall clinical stage. Crosstabulation data of clinical and pathological overall stages are presented in ►**Table 2**. The most frequent upstaging was cII to pIII or cIII to pIVa, while cIVa was the stage that registered more downstaging events.

Factors that could be associated with discrepancies were evaluated and are reported on ►**Table 3**. There was a significant association with clinical overall stage, in which overall stages cII and cIII had a disagreement on clinical and pathological findings in 75 and 70% of the cases, respectively, with a higher chance of pathological upstaging when compared with downstaging ($p = 0.006$). We have found no association between staging discrepancies and gender ($p = 0.787$), age ($p = 0.060$), tumor location ($p = 0.348$), histology ($p = 0.235$), previous surgery ($p = 0.149$), radiotherapy ($p = 0.569$) or chemotherapy ($p = 1.00$), disease relapse ($p = 1.00$), time from staging to surgery ($p = 0.762$), cT staging ($p = 0.637$), cN staging ($p = 0.120$), or imaging modality ($p = 0.213$).

T Staging Analysis

The agreement in clinical and pathological T stages was fair (Cohen Kappa: 0.374; $p < 0.001$) and differences were noted in 45.5% of the surgeries, of which 30.3% had a higher and 15.2% had a lower pathological stage. Crosstabulation data of clinical and pathological findings according to T stage are presented in ►**Table 2**. The most frequent upstaging events were cT1 to pT2 and cT3 to pT4a, and the most reported downstaging was cT2 to pT1.

Factors that could have an association with discrepancies in T staging were evaluated and reported on ►**Table 4**. There was a significant statistical association with histology ($p = 0.017$), clinical T stage ($p = 0.049$), and image modality ($p = 0.016$). A nonsquamous cell carcinoma histology was more prone to have a different pathological T stage; 100% of these cases were misclassified as opposed to 41% in squamous cell carcinomas. Moreover, patients that were submitted to CT and MRI before surgery had lower rates of identical staging (39.3%) when compared with CT (61.8%) or MRI (100%) alone. Regarding the clinical T stage, cT2 was the stage that most commonly reported disagreements, with a rate of disagreement of 52.4% and downstaging being more common than upstaging. There were no associations between T staging discrepancies and gender ($p = 1.00$), age ($p = 0.366$), tumor location ($p = 0.551$), previous surgery ($p = 0.203$), radiotherapy ($p = 0.725$) or chemotherapy ($p = 1.00$), disease relapse ($p = 0.688$), time from staging to surgery ($p = 0.523$), overall staging ($p = 0.368$), or cN staging ($p = 0.839$).

N Staging Analysis

Agreement between clinical and pathological N staging was moderate (Cohen Kappa: 0.422; $p < 0.001$), with differences in 38% of the surgeries, in which there was upstaging in 25.3% and downstaging in 12.7% of the pathologic findings. Crosstabulation data of clinical and pathological N stages are shown in ►**Table 2**. The most common upstaging events were cN0 to pN1 and cN2a-c to pN3b, and the most common downstaging event was cN1 to pN0. Furthermore, cN0 was upstaged to pN+ in 22.7% of the cases and cN+ was downstaged to pN0 in 22.9%.

Factors that could be associated with disagreements in clinical and pathological N staging were evaluated on ►**Table 5**. There was a statistically significant association with age ($p = 0.013$), cN stage ($p < 0.001$), and extranodal invasion ($p < 0.001$). In the present study, younger patients tended to be pathologically downstaged and older patients to be upstaged. Furthermore, cN0 and cN2a were identical to pathological stages in ~ 75% of the cases, while cN1 and cN2c were only identical in ~ 30% of the surgeries, and ~ 90% of the patients with positive extranodal invasion where upstaged on pathological findings. There were no associations between N staging disagreements and gender ($p = 0.407$), tumor location ($p = 0.273$), histology ($p = 0.861$), previous surgery ($p = 0.137$), radiotherapy ($p = 0.625$) or chemotherapy ($p = 1.00$), disease relapse ($p = 0.216$), time from staging to surgery ($p = 0.346$), clinical overall staging ($p = 0.107$), cT staging ($p = 0.203$), or imaging modality ($p = 0.786$).

Survival Analysis

Among the 79 patients submitted to surgery, 26 (32.9%) died with a mean time to death of 42.98 months, and 20 (25.3%)

Table 2 Concordance of pathological and clinical findings according to overall stage (2A), T stage (2B), and N stage (2C)

2A - Clinical overall stage ($n = 66$)	Pathological overall stage					Total
	pI	pII	pIII	pIVa	pIVb	
cI	10	4	4	1	0	19
cII	2	3	5	2	0	12
cIII	2	0	3	4	1	10
cIVa	1	2	3	15	3	24
cIVb	0	0	0	1	0	1
Total	15	9	15	23	4	66
2B - Clinical T stage ($n = 66$)	**Pathological T stage**					**Total**
	pT1	pT2	pT3	pT4a	pT4b	
cT1	15	7	2	1	0	25
cT2	6	10	4	1	0	21
cT3	1	0	6	4	0	11
cT4a	0	2	1	5	1	9
Total	22	19	13	11	1	66

2C - Clinical N stage ($n = 79$)	Pathological N stage							Total
	PN0	pN1	pN2a	pN2b	pN2c	pN3a	pN3b	
CN0	34	7	0	2	0	0	1	44
cN1	4	3	0	1	0	0	2	10
cN2a	0	0	3	0	0	0	1	4
cN2b	3	0	0	7	1	0	2	13
cN2c	1	0	0	1	2	1	2	7
cN3a	0	0	0	1	0	0	0	1
Total	42	10	3	12	3	1	8	79

Table 3 Factors associated with clinical and pathological overall staging disagreements

Overall staging comparison				
	Identical ($n = 31$)	Upstaging ($n = 24$)	Downstaging ($n = 11$)	*p-value*
Gender				
Female ($n = 8$)	62.5%	25%	12.5%	0.787
Male ($n = 58$)	44.8%	37.9%	17.2%	
Age (mean ± SD)	60.10 ± 13.10	59.04 ± 12.20	49.36 ± 13.89	0.060
Local				
Oral cavity ($n = 23$)	30.4%	47.8%	21.7%	0.348
Pharyngeal ($n = 11$)	54.5%	36.4%	9.1%	
Laryngeal ($n = 26$)	61.5%	26.9%	11.5%	
Others ($n = 6$)	33.3%	33.3%	33.3%	
Histology				
Squamous cell carcinoma ($n = 61$)	49.2%	36.1%	14.8%	0.235
Others ($n = 5$)	20%	40%	40%	
Clinical overall staging*				**0.006**
Imaging				
CT ($n = 34$)	55.9%	35.3%	8.8%	0.213
MRI ($n = 3$)	66.7%	33.3%	0	
CT+ MRI ($n = 28$)	32.1%	39.3%	28.6%	
PET ($n = 1$)	100%	0	0	

Abbreviation: SD, standard deviation.

Table 4 Factors associated with clinical and pathological T staging disagreements

T Staging Comparison				
	Identical ($n = 36$)	**Upstaging ($n = 20$)**	**Downstaging ($n = 10$)**	***p-value***
Gender				
Female ($n = 8$)	62.5%	25%	12.5%	1.00
Male ($n = 58$)	53.4%	31%	15.5%	
Age (mean ± SD)	59.67 ± 12.17	57.25 ± 14.097	53 ± 15.51	0.366
Location				
Oral cavity ($n = 23$)	47.8%	26.1%	26.1%	0.551
Pharyngeal ($n = 11$)	63.6%	27.3%	9.1%	
Laryngeal ($n = 26$)	61.5%	30.8%	7.7%	
Others ($n = 6$)	33.3%	50%	16.7%	
Histology				**0.017**
Squamous cell carcinoma ($n = 61$)	59%	27.9%	13.1%	
Others ($n = 5$)	0	60%	40%	
Clinical T Staging*				**0.049**
Imaging				
CT ($n = 34$)	61.8%	35.3%	2.9%	**0.016**
MRI ($n = 3$)	100%	0	0	
CT + MRI ($n = 28$)	39.3%	28.6%	32.1%	
PET-CT ($n = 1$)	100%	0	0	

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; PET-CT, positron emission tomography/computed tomography; SD, standard deviation.

Table 5 Factors associated with clinical and pathological N staging disagreements

N staging comparison				
	Identical ($n = 49$)	**Upstaging ($n = 20$)**	**Downstaging ($n = 10$)**	***p-value***
Gender				
Female ($n = 8$)	87.5%	12,5%	0	0.407
Male ($n = 71$)	59.2%	26.8%	14.1%	
Age (mean ± SD)	58.22 ± 12.80	63.90 ± 10.08	49.20 ± 15.78	**0.013**
Local				
Oral cavity ($n = 26$)	50%	30.8%	19.2%	0.273
Pharyngeal ($n = 13$)	46.2%	38.5%	15.4%	
Laryngeal ($n = 28$)	75%	14.3%	10.7%	
Others ($n = 12$)	75%	25%	0	
Histology				
Squamous cell carcinoma ($n = 72$)	61.1%	26.4%	12.5%	0.861
Others ($n = 7$)	71.4%	14.3%	14.3%	
Clinical N staging *				< **0.001**
Extraganglionar invasion				
Yes ($n = 9$)	11.1%	88.9%	0	< **0.001**
No ($n = 70$)	68.6%	17.1%	14.3%	
Imaging				
CT ($n = 40$)	65%	25%	10%	0.786
MRI ($n = 7$)	57.1%	14.3%	28.6%	
CT + MRI ($n = 30$)	56.7%	30%	13.3%	
PET-CT ($n = 1$)	100%	0	0	

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; PET-CT, positron emission tomography/computed tomography; SD, standard deviation.

relapsed with a mean time to recurrence of 42.65 months. Even though none of the patients was lost to follow-up, the median follow-up among living patients was 19 months (2 to 115 months).

Using the Kaplan-Meyer method, we found no significant differences in 5-year overall survival and 5-year disease-free survival between the groups with identical, upstaging, or downstaging on pathological T, N or overall staging.

Discussion

Our primary objective was to assess and compare clinical and pathological overall, T, and N staging in HNC and we found a fair to moderate level of agreement.[16] When managing oncological patients after clinical staging, clinicians should be aware that staging disagreements occur in $\sim$ 50% of the cases, be alerted of the most common staging disagreements, and understand why they occur. In the present paper, we have analyzed which are the most common staging disagreements and tried to propose an explanation for their occurrence. The most common T staging disagreements were cT3 to pT4a, cT1 to pT2 and cT2 to pT1, and tumors with a nonsquamous cell histology showed a tendency for T staging discrepancies. Furthermore, the most common N staging disagreements were cN2a-c to pN3b, cN0 to pN1 and cN1 to pN0, and the presence of extranodal disease or older age at presentation were associated with upstaging events while younger age at presentation was associated with downstaging events.

The age at presentation and male predominance in the present study were similar to what has been previously presented.[8,9,11,13,15] On the other hand, tobacco and alcohol consumption were not as frequent as previously reported,[8,9,11] probably due to lack of information on clinical data. The clinical staging in this population was I/II in 39.3% and III/IV in 60.7%, which is more balanced when compared with previous studies with a higher inclusion of advanced disease[8,9,11] or with another study with a higher rate of initial stages of the disease.[12]

Discrepancies were noted in 53% of the cases in overall staging, in 45.5% in T staging, and in 38% in N staging, which correlates well with previously published studies considering head and neck squamous cell carcinoma.[7,9] Overall, pathological upstaging was twice more common when compared with pathological downstaging. Other studies have compared clinical and pathological staging agreements on specific sites such as oral cavity cancer or laryngeal cancer. Regarding oral cavity cancers, disagreements on T staging have been reported as ranging from 12.7 to 55.9%,[12,14,15] and disagreements on N staging from 17.5 to 69.5%.[8,12,14,15] In the present study, there was a 47.8% disagreement on T staging and 50% on N staging for oral cavity cancer. Furthermore, regarding laryngeal cancer, there was an agreement in both T staging and overall staging of 61.5% and on nodal staging of 75%, which are similar to those previously reported.[11] Even though Celakovsky et al. found a similar agreement on nodal staging, they found a higher agreement on T staging of 85.5%.[13]

Overall staging disagreements were associated with clinical overall staging, in which cII and cIII had a disagreement in almost three quarters of the cases, with upstaging from cII to pIII and from cIII to pIVa being the most common causes of disagreement.

T staging discrepancies were associated with histology. Nonsquamous cell carcinoma had different clinical and pathological stages in 100% of the cases and upstaging was more common than downstaging. Thus, it seems that the size and depth of cancer penetration are easier to assess on imaging exams in squamous cell carcinomas when compared with other histological types. There was also an association with imaging modality in which patients submitted to both MRI and CT had a higher chance of staging disagreements. Furthermore, MRI or PET-CT were the most precise imaging modalities, with 100% accuracy, but it should be noted that only 3 patients were submitted to the former and only 1 to the latter. Eder-Czembirek et al.[7] did not find an association between imaging modality and disagreements between stagings. Thus, we hypothesize that both CT and MRI were performed to patients with tumors that were more difficult to assess in an isolated imaging modality, which may have led to bias. There was also an association with clinical T stage, in which one of the most common upstaging events was from cT3 to pT4a, which suggests that there is some underestimation of the extent of invasion of critical structures, which varies depending on primary site of cancer. On laryngeal cancer, there could be an underestimation of growth through the cricoid and thyroid cartilages or growth to structures beyond the larynx. Previous studies show that CT fails to identify cartilage invasion in up to 40% of the cases[17,18] and that cT3 tumors are upstaged to pT4 in up to 33% of the cases.[19] On the other hand, Kılıç et al. previously reported similar findings on oral cavity cancer, in which there could be an underestimation of the invasion of cortical bone, of the deep muscle of the tongue, of the maxillary sinus, or of the skin of the face.[12] Upstaging from cT1 to pT2 and downstaging cT2 to pT1 were frequent, which suggests there is also some difficulty to estimate tumor size and depth of invasion in the earlier stages of the disease.

Regarding nodal staging, there was an association between staging disagreements and age, clinical nodal stage, or extranodal invasion. As aforementioned, cN1 and cN2c only had an agreement in pathological stagings of around one third of the cases, in which cN2c was upstaged to pN3b in almost one third of the cases. Furthermore, there was an important number of upstaging events from cN+ to pN3b. This is in accordance with the finding that almost 90% of the patients with extranodal invasion were upstaged on pathological findings, which suggests that imaging is not accurate enough to predict extranodal invasion, leading to an important number of staging disagreements. Imaging modalities cannot assess accurately micrometastasis either, which altogether leads to a rate of false negatives in 20 to 30% of the cases,[20,21] which is in accordance with the 22.7% rate of occult nodal metastases in the present study. A rate of 31.3% of occult nodal metastasis was previously reported in patients with HNC,[9] 34% in oral tongue cancer,[22] 36% in

the ipsilateral neck, and 27% on the contralateral neck in cases of laryngeal and hypopharyngeal cancer.[23] The most frequent downstaging event was from cN1 to pN0, which shows some difficulty to differentiate small reactive nodes from pathological nodes on imaging alone. This could also explain an association between earlier age at presentation and downstaging events, since there could be a higher rate of reactive nodes in younger patients, which could result on false cN+ stages. Kılıç et al. have also reported that advanced age was associated with higher upstaging events but they did not report an association with downstaging events.[12] Nodal disagreements can also result from an incomplete nodal yield during neck dissection or from pathological assessment methods. In this cohort, the mean nodal yield on primary ND was 19.5, which is in accordance with the number published by another group.[24]

In both overall, T, and N stagings, there was no association with gender, primary tumor site, previous surgical or adjuvant treatment, recurrent disease, or time from staging to surgery in months. Although a higher time to surgery is expected to result in tumor progression with a higher rate of upstaging events, there was no association in this cohort, neither in a cohort of patients with larynx cancer.[11] However, Kılıç et al. found that, in oral cavity squamous cell carcinoma, there was a higher rate of upstaging in patients with a time to treatment of 4 to 8 weeks when compared with patients who started treatment in < 4 weeks after diagnosis. They also found a higher rate of upstaging in higher histological grades or with a higher number of lymph nodes on pathological specimens.[12] It was to be expected that cases of recurrent disease would be harder to stage accurately; however we did not find any association with staging disagreements in these cases, as has been previously reported.[9]

We didn't find differences in five-year survival or disease-free survival. However, even though this cohort did not have patients lost to follow-up, the median follow-up time was only 19 months (2 to 115 months), since many surgeries (17.7%) where performed < 1 year prior to data collection. Thus, the survival analysis may have been biased by the significant number of censored patients, even though there was a similar censored rate among all groups. Previous reports have also showed no differences in mortality or disease-free survival among groups,[9,11,14,15] which may be explained by treatment adjustments according to pathological staging, in which upstaging a patient may enable appropriate adjuvant treatment and downstaging a patient may prevent unnecessary morbidity from excessive adjuvant treatment. On the other hand, other retrospective studies have shown increased mortality on pathological T upstaging,[13] nodal upstaging,[8] or both.[12] More studies are still needed to enlighten the role of staging discrepancies in overall and disease-free survival.

The present study has several limitations. It is a retrospective analysis with all its known limitations. It included patients who underwent ND in the same institution, but they were operated by different head and neck surgeons, and specimens were analyzed by different pathologists. On the other hand, this may enable a more realistic representation of staging disagreements in general clinical practice. In addition to this, to find associations with staging disagreements and to have a larger sample, inclusion criteria were drafted for a greater inclusivity, leading to a heterogeneous group including patients with cancer from different head and neck sites, different cancer histologies, patients submitted to revision surgery, or treated previously with radiotherapy or chemotherapy. Furthermore, a multivariate analysis was not possible because the sample of the present study was not large enough. Regarding survival analysis, the small follow-up time was a limitation.

Conclusion

Overall, T, and N staging disagree in an important number of cases; overall stage can disagree in up to 53% of the cases and upstaging seems to be twice as frequent as downstaging events. Imaging modalities are not accurate enough in predicting tumor invasion to vital structures, estimating tumor size in the earlier stages or in assessing micrometastasis or extranodal invasion, playing a major role on staging disagreements. Although upstaging and downstaging events do not seem to influence overall and disease-free survival, more studies are still needed to enlighten the role of staging discrepancy on survival.

Funding
The author(s) received no financial support for the research.

Conflict of Interests
The authors have no conflict of interests to declare.

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