RESEARCH

Comparison between computed tomography and clinical evaluation in tumour/node stage and follow-up of oral cavity and oropharyngeal cancer

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Objectives: The aim was to verify the concordance of CT evaluation among four radiologists (two oral and maxillofacial and two medical radiologists) at the TN (tumour/node) stage and in the follow-up of oral cavity and oropharyngeal cancer patients. The study also compared differences between clinical and CT examinations in determining the TN stage.

Methods: The following clinical and tomographic findings of 15 non-treated oral cavity and oropharyngeal cancer patients were compared: tumour size, bone invasion and lymph node metastases. In another 15 patients, who had previously been treated, a clinical and tomographic analysis comparison for the presence of tumoural recurrence, post-therapeutic changes in muscles and lymph node metastases was performed. The concordances of tomographic evaluation between the radiologists were analysed using the kappa index.

Results: Significant agreement was verified between all radiologists for the T stage, but not for the N stage. In the group of treated patients, CT disclosed post-therapeutic changes in muscles, tumour recurrence and lymph node metastases, but no concordance for the detection of lymph node metastases was found between radiologists. In the first group, for all radiologists, no concordance was demonstrated between clinical and tomographic staging. CT was effective for delimitating advanced lesions and for detecting lymph node involvement in N0 stage patients. CT revealed two cases of bone invasion not clinically detected.

Conclusions: Interprofessional relationships must be stimulated to improve diagnoses, and to promote a multidisciplinary approach to oral cavity and oropharyngeal cancer. Although CT was important in the diagnosis and follow-up of cancer patients, differences between medical and dental analyses should be acknowledged.

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Introduction

Squamous cell carcinoma of the oral cavity and oropharynx accounts for 2–6% of all the malignant neoplasms and consistently ranks among the top ten prevalent cancers worldwide. Geographic variations in incidence and mortality have been observed partly because of the prevalence of known aetiological risk factors, such as tobacco use.^{1–3} Although significant improvements in head and neck cancer therapy have

been observed over the last decades, some authors have stated that the final survival rates were not significantly influenced by the advent of new approaches.^{4,5} On the other hand, in some documented cases, the estimated survival rates have shown remarkably good results with pre-operative chemoradiotherapy (CRT) and radical surgery.⁶ However, these findings are based on data from a large proportion of studies using consecutive patient series. To date, hard evidence providing sufficient data from prospective randomized studies is lacking for pre-operative CRT. Prospective randomized studies are mandatory in this area. Therefore, efforts

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are necessary to better diagnose, treat and follow up head and neck cancer patients.

A multidisciplinary approach is essential for head and neck cancer. It generally begins at the moment of referral to a health centre and continues throughout cancer treatment and subsequently during any further rehabilitation procedure.⁷ As dentists and physicians generally perform the initial diagnosis and follow-up of oral cavity and oropharyngeal cancer, it is important to compare the evaluation differences of these professionals. The outcome of the initial diagnosis is affected mainly by the stage of the disease at the time of the examination. The tumour, node, metastasis (TNM) classification provides a reliable basis for patient prognosis and therapeutic planning.⁸ The staging of cervical lymphadenopathy may be considered one of the most significant factors in determining patients' prognoses.⁹ Clinical examination alone is not sufficient to evaluate lymph node involvement in head and neck cancer. Some authors have demonstrated that over 20% of neck palpation-negative patients have indeed occult neck metastases.^{10,11} Another important factor for accurately estimating survival is a long-term follow-up of patients with oral malignancies.¹² Local recurrent tumours following primary treatment are a relatively common occurrence after treatment, and are, sometimes, also not detected clinically.¹³

Imaging examinations can provide key information for the adequate staging of oral cancer patients, such as depth or extent of invasion, bone invasion and evaluation of regional lymph nodes. The imaging modalities include CT, MRI, nuclear medicine scintigraphy, ultrasound and positron emission tomography (PET).¹⁴ As CT is more widely available and less expensive, it is a standard imaging technique for head and neck tumours.^{15,16} In Brazil, both oral and maxillofacial radiologists (OMFRs) and medical radiologists are able to evaluate CT examinations. No other study was found in the literature comparing tumour/node (TN) stage evaluations among professionals from different training backgrounds. The main objective of this study was to verify the differences between tomographic analyses performed by oral and medical radiologists. This study also compared differences between clinical and tomographic evaluation in TN stage definition and in the follow-up of oral cavity and oropharyngeal cancer patients.

Materials and methods

The subjects were 30 patients with oral cavity and oropharyngeal squamous cell carcinoma referred to the Oral Cancer Center of the University of Brasilia Hospital, between October 2005 and February 2007. There were 23 men and 7 women aged between 24 and 79 years (mean age 58 years). 26 patients consumed alcohol and 26 also smoked tobacco. The study was

approved by the local research ethics committee and informed consent was obtained from all participants.

The sample was divided into two groups of patients with histologically proven squamous cell carcinoma. The first group included 15 patients without previous treatment. The second group consisted of 15 patients who had previously undergone surgery, radiotherapy or chemotherapy. Patients who were not able to receive intravenous contrast, such as those with multiple myeloma, kidney diseases and allergies, were excluded from the study.

All of the selected patients underwent clinical and tomographic examinations. In each studied group, a head and neck surgeon performed the clinical staging, according to the TNM criteria.¹⁷ Four radiologists, two OMFRs (observers 1 and 2) with 7 years of experience, and two medical radiologists (observers 3 and 4), with 5 years of experience with cancer patients, analysed the images in order to evaluate interobserver agreement.

The size of the tumour (T stage), the lymph node involvement (N stage), the presence of bone invasion and the level of involved lymph nodes were evaluated by both clinical and tomographic examination in the first group. In the second group, the radiologists evaluated the presence of lymph node metastases, tumoural recurrence and post-therapeutic changes in muscles. In both groups, the radiologists were blind to the clinical features of each patient and they were also unaware of the other radiologists' reports.

CT

The patients were examined in a multislice CT Lightspeed QX/I (GE, Milwaukee, WI), located at the imaging centre of the university hospital. The region of interest extended from the base of the skull to the upper mediastinum. Scanning was performed in the axial plane at 120 kVP and 250 mA. Slice thickness was 1.3 mm and 0.8/s table feed, using a display matrix of 512 × 512. The patients were scanned in the supine position (gantry tilt, 22°). Contrast material enhancement was achieved by intravenous manual administration of non-ionic contrast material (Iopamiron 300, Schering, Brazil). An intravenous dose of 50 ml of the contrast was administered at the start of scanning and an additional 50 ml infusion was performed during the scanning to allow better visualization of the vascular structures.

Tomographic assessment followed the parameters below:

- using soft-tissue and bone windows to analyse, respectively, soft-tissue involvement and bone invasion
- visualization of contrast enhancement
- presence or absence of cervical lymph node metastases, following criteria proposed by Prehn *et al*¹⁸
- delineation of lymph node levels, following criteria proposed by Som *et al*¹⁹

Table 1 Clinical data of non-treated patients (group 1)

Patient no.	Gender	Age	Smoker	Alcohol	Clinical TNM	Primary site
1	Male	48	Yes	Yes	T2N1M0	Oropharynx
2	Female	50	No	No	T2N0M0	Gingiva
3	Male	55	Yes	Yes	T2N1M0	Retromolar region
4	Male	51	Yes	Yes	T4N2M0	Floor of mouth
5	Male	76	Yes	Yes	T4N0M0	Oropharynx
6	Male	52	Yes	Yes	T3N2M0	Oropharynx
7	Female	79	No	No	T1N0M0	Retromolar region
8	Female	48	Yes	Yes	TisN0M0	Tongue
9	Female	52	Yes	No	T2N0M0	Oropharynx
10	Male	46	Yes	Yes	T4N3M0	Floor of mouth
11	Male	66	Yes	Yes	T1N0M0	Floor of mouth
12	Female	50	Yes	No	T1N0M0	Floor of mouth
13	Male	45	Yes	Yes	T1N0M0	Floor of mouth
14	Male	62	Yes	Yes	T1N0M0	Tongue
15	Male	42	Yes	Yes	T4N2M0	Tongue

The archived CT data, originally stored on optical disks, were transferred to an independent workstation Satellite (Toshiba, Japan) with eFilm 2.0 software (Merge Technologies, Milwaukee, WI) for manipulation, analysis and interpretation. All images were analysed on eFilm, and the staging based on TNM criteria.¹⁷

Statistical methods

In the first group, the concordance between the clinical and tomographic analyses for the size of the tumour (T stage), lymph node involvement (N stage), presence of bone invasion and the level of involved lymph nodes, as well as the interobserver tomographic agreement for those variables, were evaluated using Cohen's kappa index. The kappa index was also used in the second group to evaluate concordance between the clinical and tomographic data for the presence of tumoural recurrence and lymph node metastases, and also to analyse interobserver tomographic agreement for the presence of tumoural recurrence, post-therapeutic changes in muscles and cervical metastases. All analyses were carried out using SPSS for Windows 13.0 (SPSS, Chicago, IL). *P*-values of less than 0.05 were considered statistically significant.

Results

The main clinical features of the first and second groups are reported in Tables 1 and 2, respectively. The distribution of patients by primary site of squamous cell carcinoma was oropharynx (10 cases, 33.3%), floor of the mouth (9 cases, 30%), tongue (7 cases, 23.4%), retromolar region (3 cases, 10%) and gingival region (1 case, 3.3%).

Concordance between analyses performed by the four radiologists in the first group (non-treated patients)

Comparing the four radiologists (two OMFRs and two medical radiologists), there was concordance in determining the tumour size. On the other hand, no concordance was found for identifying the staging and the N stage (Table 3).

The CT-based delineation of lymph node levels was performed by all radiologists, and no interobserver agreement was found for this analysis ($P > 0.05$).

No significant interobserver concordance was found between clinical and tomographic staging for the OMFRs or the medical radiologists (Table 4). Concordance was also not demonstrated between clinical and tomographic

Table 2 Clinical data of treated patients (group 2)

Patient no.	Gender	Age	Smoker	Alcohol	Clinical TNM	Primary site	Treatment	Tumoural recurrence
1	Female	24	No	Yes	T1N2M0	Oropharynx	Surgery and radiotherapy	No
2	Male	75	Yes	Yes	T2N0M0	Oropharynx	Radiotherapy	No
3	Male	61	Yes	Yes	T1N0M0	Tongue	Surgery and radiotherapy	No
4	Male	48	Yes	Yes	T4N1M0	Oropharynx	Surgery	Yes
5	Male	60	Yes	Yes	*	Floor of mouth	Surgery and radiotherapy	No
6	Male	41	No	Yes	T4 N1M0	Tongue	Radio- and chemotherapy	No
7	Male	56	Yes	Yes	T2N1M0	Oropharynx	Surgery and radiotherapy	No
8	Male	56	Yes	Yes	T2N0M0	Oropharynx	Radiotherapy	No
9	Male	68	Yes	Yes	T2N1M0	Floor of mouth	Surgery and radiotherapy	No
10	Male	63	Yes	Yes	T2N1M0	Floor of mouth	Surgery and radiotherapy	No
11	Male	62	Yes	Yes	T2N0M0	Tongue	Surgery	Yes
12	Female	52	Yes	Yes	T3N2M0	Tongue	Surgery and radiotherapy	No
13	Male	78	Yes	Yes	T2N0M0	Retromolar region	Surgery	No
14	Male	61	Yes	Yes	*	Oropharynx	Radio-, chemotherapy and surgery	No
15	Male	59	Yes	Yes	T2N0M0	Floor of mouth	Radio-, chemotherapy and surgery	No

*Data not available in medical records

Table 3 Concordance of tomographic evaluation of tumour/node (TN) stage between oral and maxillofacial radiologists (OMFRs) and medical radiologists in non-treated patients (first group)

Interobserver agreement	T stage	N stage	Staging
OMFR 1 × OMFR 2	Kappa = 1 ($P < 0.001$)	$P = 0.795$	$P = 0.161$
OMFR 1 × medical radiologist 1	Kappa = 0.896 ($P < 0.001$)	$P = 0.114$	$P = 0.315$
OMFR 2 × medical radiologist 1	Kappa = 0.896 ($P < 0.001$)	$P = 0.245$	$P = 0.486$
OMFR 1 × medical radiologist 2	Kappa = 0.426 ($P < 0.001$)	$P = 0.133$	$P = 0.295$
OMFR 2 × medical radiologist 2	Kappa = 0.511 ($P < 0.001$)	$P = 0.130$	$P = 0.320$
Medical radiologist 1 × medical radiologist 2	Kappa = 0.511 ($P < 0.001$)	$P = 0.144$	$P = 0.177$

For all kappa values, $P < 0.05$ = concordance

evaluations (performed by both radiologists) when the size of the tumour (T) and the presence of cervical lymph node metastases (N) were analysed separately. There was a higher number of concordances for T4 tumours. The evaluation of the size of the tumour was based on contrast enhancement (Figure 1). The analysis of the N stage was based on the presence of central necrosis and the size of the lymph node (Figure 2). Clinical evaluation yielded more negative necks than did tomography.

Two patients presented bone invasion (Figures 3 and 4), which was detected by all radiologists.

Concordance between analyses performed by the four radiologists in the second group (treated patients)

There was no interobserver concordance for the analysis of cervical lymph node metastases either between the oral radiologists or between the oral radiologists and the medical radiologists or even between the medical radiologists ($P > 0.05$).

There was a perfect concordance among all radiologists for the detection of tumoural recurrence (kappa = 1, $P < 0.001$). All radiologists also detected hypodensities of muscles in two patients, a post-therapeutic change probably related to the transformation of muscle into fatty tissue (Figure 5).

There was a high concordance between clinical and tomographic evaluation of the presence of tumoural recurrence (kappa = 0.86, $P < 0.001$) for all examiners. Three patients showed tumoural recurrence at both clinical and tomographic examinations. Those cases of tumoural recurrence were confirmed by histopathology. Two cases of tumoural recurrence were suspected only after contrast-enhanced tomography (Figure 6). None of the patients presented osteoradionecrosis. No concordance was demonstrated between clinical and tomographic identification of lymph node metastases for either of the radiologists ($P > 0.05$). No significant concordance was found for the evaluation of the level of involved lymph nodes ($P > 0.05$).

Discussion

Although modern techniques, such as PET, have proven to be more effective in the evaluation of oral cancer patients,²⁰ CT is one of the most widely available techniques. This study was undertaken to verify variability in CT evaluation between medical and dental professionals, both involved in the primary diagnosis of oral cancer. The role of CT on staging and follow-up of oral cavity and oropharyngeal squamous cell carcinoma patients is also discussed below.

No agreement was determined for CT-based delineation of lymph node levels in both groups of treated and non-treated patients (Tables 3 and 4). Further studies are needed to confirm the poor reproducibility of this analysis.

Regarding interobserver agreement for the tomographic evaluation, a perfect concordance was found between the OMFRs in identifying the tumour size. Concordance was also verified between OMFRs and medical radiologists. The lack of concordance for tomographic staging analysis may be due to the lack of agreement in N-stage determination. Further studies are necessary to clarify whether there are differences in evaluation of lymph node metastases between radiologists from different training backgrounds. It was not possible to explain the differences found in the tomographic analysis of cervical lymphadenopathy, although these may be related to the sample size or the difficulty of identifying lymph node involvement. It should be mentioned that dental professionals are less experienced in evaluating neck areas, which may hinder the analysis of lymph nodes located in these regions. For both professionals, the diagnosis of lymph node metastases (N stage) seems to be more complex than the determination of tumour size.

For the tomographic evaluation of follow-up patients (group 2), a perfect concordance was found between OMFRs and medical radiologists in detecting

Table 4 Comparison between clinical and tomographic staging in non-treated patients performed by radiologists (oral and maxillofacial radiologists (OMFRs) and medical radiologists)

Concordance between clinical and tomographic examination	T stage	N stage	Staging
Clinical × first OMFR	$P = 0.106^*$	$P = 0.795^*$	$P = 0.161^*$
Clinical × second OMFR	$P = 0.602^*$	$P = 0.613^*$	$P = 0.106^*$
Clinical × first medical radiologist	$P = 0.326^*$	$P = 0.167^*$	$P = 0.136^*$
Clinical × second medical radiologist	$P = 0.068^*$	$P = 0.590^*$	$P = 0.078^*$

*For all kappa values, $P < 0.05$ = concordance

Figure 1 Contrast enhancement on CT. Stage 2 tumour at the mouth floor and base of the tongue (white arrowheads). The patient was clinically staged as T1

post-therapeutic changes in muscles and tumoural recurrence. No concordance was found among the radiologists for the analysis of lymph node metastases. In post-treatment patients, the differences may be also related to the post-therapeutic changes that alter the normal anatomy, tissue planes and landmarks.²¹

As diagnosis of oral cancer is usually performed by physicians or dentists, the weak concordance shown here regarding tomographic analyses is a serious concern. Therefore, interprofessional relationships should be encouraged not only to improve diagnoses, but also to promote a multidisciplinary approach to oral cavity and oropharyngeal cancer treatment. Further studies are thus necessary to confirm the reproducibility of tomographic staging through adequate training of different examiners and consensus among professionals. Intraobserver differences should also be analysed in future investigations.

Interobserver agreement was found in tomographic evaluations for the T stage, but not for the N stage (Table 3). No concordance was found between clinical and tomographic staging for patients without previous treatment (Table 4). When the size of the tumour was analysed separately (T stage), there was a higher number of concordances for T4 tumours. This result suggests that larger tumours are more easily detected by both clinical and tomographic evaluations. On the other hand, two cases of *in situ* carcinomas were only clinically detected. Moreover, one carcinoma staged as T1 by clinical examination was staged as T0 by tomography. This indicates that CT may fail to reveal lesions in early stages as suggested by previous studies.^{22,23} According to Lenz *et al*,²⁴ small T1-stage tumours of the oral cavity and oropharynx are detected by CT only if they show an enhancement after intravenous contrast medium application. Frequently beam-hardening artefacts, caused by dense bones and teeth or by metal dental fillings, may interfere with the CT image.

a

b

Figure 2 Imaging of metastatic lymph nodes (white arrows) based on the presence of central necrosis (a) and size >10 mm (b)

Figure 3 Patient with clinically T4N0 oropharynx carcinoma, classified as T4aN2c by CT. (a) Axial scan (soft-tissue window) reveals the lesion in soft palate with contrast enhancement (white arrowheads). (b) Magnified image of a sagittal multiplanar reconstruction disclosing the lesion below the left maxillary sinus (white arrowheads). (c) Coronal multiplanar reconstruction demonstrating metastatic lymph node level IB with central necrosis (white arrow) and the primary tumour (arrowheads). (d) Coronal reconstruction (bone window) revealing bone destruction at the floor of the left maxillary sinus (black arrow)

In the present study, the cases of bone invasion were identified by all radiologists. Although some authors have not found significant differences between clinical and tomographic evaluation of bone invasion,²⁵ other researchers have pointed out that CT may be able to detect small cortical erosions, usually not detected by

clinical examination or by plain radiographs.²⁶ The pattern of bone destruction may influence the outcome of squamous cell carcinoma.²⁷

In the present study, clinical evaluation yielded more negative necks than tomography. When CT was used, metastatic involvement of the lymph nodes was observed.

a

b

Figure 4 Clinically staged T4N3 carcinoma at the mouth floor, staged T4N2c by CT. (a) Axial CT (soft-tissue window) showing contrast enhancement (white arrowhead). (b) Axial scan (bone window) showing bone invasion with destruction of buccal and lingual cortices (black arrow)

However, the accuracy of the imaging modalities in detecting these metastases remains controversial in the literature.^{28,29} In comparison with clinical examination, CT seems to detect cervical lymphadenopathy better.

However, we lack histological proof after lymph node dissection to support this assertion.

In the follow-up patients (second group), two cases of tumoural recurrence were detected by clinical and

a

b

Figure 5 (a) Axial scan, soft-tissue window. Contrast enhancement suggesting tumoural recurrence at the tongue (black arrowheads). (b) Patient with resected carcinoma of the tongue with hemiglossectomy and contrast enhancement denoting tumoural recurrence (black arrowhead). Note metastatic lymph node, level IIIA (white arrow), and absence of left jugular vein, probably due to neck dissection

Figure 6 (a, b) Hypointense areas indicating muscle changes, probably due to denervation, muscle atrophy and consequent change of muscle into fatty tissue (arrows)

tomographic examination that explain the perfect agreement between clinical and tomographic evaluation ($\kappa = 1$, $P < 0.05$) for all observers. The tomographic analysis was based on the detection of infiltrate mass with contrast enhancement. Subsequently, both cases were histopathologically confirmed. Some authors have demonstrated that CT may be useful in differentiating tumoural recurrence from post-therapeutic changes.^{30,31} On the other hand, as mentioned by other authors,^{32,33} we agree that the diagnosis of recurrent tumour is more difficult in both clinical and imaging modalities because of possible changes related to oral cavity and oropharyngeal cancer treatment, such as inflammatory and post-therapeutic changes in muscles and anatomical alterations after tumour removal or radical neck dissection. In the present study, both oral and medical radiologists were able to detect and

differentiate post-therapeutic changes in muscles from recurrent tumours, as may be found in the literature.

In conclusion, differences between clinical and tomographic analyses should be recognized. Interprofessional relationships must be stimulated to improve diagnoses, and to promote a multidisciplinary approach to oral cavity and oropharyngeal cancer. CT is an important tool in the diagnosis and follow-up of patients with oral cavity and oropharyngeal cancer, but may also have limited capacity in identifying metastatic lymph nodes. Further studies with different imaging modalities are necessary for the evaluation of malignant cervical lymphadenopathy, in comparison with histopathological analyses after neck dissection. The early detection of lymph node metastases may be considered one of the most important objectives because it could affect the survival rate of cancer patients.

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