Prognostic implications of node metastatic features in OSCC: A retrospective study on 121 neck dissections

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Abstract. Lymph node metastases are responsible for shorter survival in oral squamous cell carcinoma (OSCC). The aim of the present study was to assess the node metastasis frequency and survival according to the node metastasis features in 121 neck dissections (NDs) performed for OSCC, identifying evidence-based correlations and contrasts with previous literature. The retrospective study involved 121 patients affected by OSCC who had undergone modified radical ND (MRND) for therapeutic, elective reasons or after intraoperative positivity to metastasis of sentinel lymph nodes (SLN+). Node metastasis frequency and behaviour (typical vs. atypical) and their number and distribution according to pre-surgical cTNM cancer staging were considered and overall survival Kaplan-Meier curves were calculated for each group in order to compare mortality according to ND type (elective, therapeutic, after SLN+), lymph node metastatic pattern (typical or atypical), size (micrometastasis vs. macrometastasis) and number. Results showed statistically significant different overall survival according to pre-surgical staging, number of lymph nodes harvested and intent to surgery. Sentinel lymph node resulted in the sole positive node affected by metastasis in small cT1- cT2/cN0 OSCC and an ND subsequent to its positivity during intraoperative assessment may be considered an overtreatment.

Introduction

Oral squamous cell carcinoma (OSCC) is the sixth most common cancer internationally, accounting for ~5% of all malignant tumours worldwide (1). OSCCs commonly metastasize to cervical lymph nodes. Each tumour generally metastasizes in a particular group of cervical lymph nodes and the principles and criteria governing neck dissection (ND) are based on the primary tumour characteristics, according to the cTNM staging and its primary site (2,3).

Cervical lymph node metastases (LNMs) are key malignancy criteria in OSCC (4). Their presence influences the therapeutic plan and prognosis, since it is associated with a 50% decrease in survival (5,6).

The selection of OSCC cases requiring ND depends mainly on the clinical TNM staging (cTNM). cTNM provides a stage
grouping based on the extent of the primary tumour (T score),
the involvement of the regional, cervical, lymph nodes (N
score) and the detection of distant metastases (M score) (2,3,7).
These parameters are accurately quantified after performing a
series of clinical-instrumental examinations such as PET, total
body CT scan, neck echo-color Doppler, fibrolaryngoscopy,
esophageal-gastric-duodenoscopy, bronchoscopy and, if any
doubts persist, fine needle aspiration biopsy (FNAB) and
biopsy must be also performed.

Once clinical T, N and M parameters have been defined, a
ND is mandatory for the OSCCs showing cervical LNMss (any
cT/N+) and for locally advanced primary tumours (cT3 or cT4)
with clinically undetectable LNMss (cN0).

Based on the intent or purpose, NDs have been also clas-
sified into therapeutic and elective. Therapeutic NDs are
performed in OSCCs with cervical metastases detected in
clinical preoperative setting (any T/N+). Elective NDs are
selected for locally advanced primary tumours (T3 or T4)
with clinically undetectable LNMss (cN0) (8). NDs are also
performed in the cases of small primary tumours clinically
negative to node involvement (cT1-T2/N0) that during intra-
operative assessment of their sentinel lymph node reveal
positivity to metastasis (9).

Both ND anatomical extent and involvement of surrounding
structures are related to the node levels involved in the dissec-
tion and they are planned on the basis of the OSCC primary
site; correlations between primary site of the cancer and level
of metastasis have been demonstrated and, to date, they aid
the surgeon in the surgical ND management (10).

Currently, NDs are classified into four basic procedures
according to the extent of different cervical lymph node groups
and surrounding structures: radical ND, modified radical ND,
(MRND) extended ND and selective ND (8,11).

Following histopathological assessment of the tumour
margins of excision and after the evaluation of the involve-
ment of the surrounding structures, adjuvant therapy may also
be performed: radiotherapy for T4 tumours with free surgical
margins and/or ≥N2; and both radiotherapy and chemother-
apy for tumours with any N+ plus extracapsular spread
(ECS) and ones with any T and positive or close margins or
perineural invasion and/or neoplastic vascular embolization.
T1-3 tumours with free margins and pN0/pN1 do not require
adjuvant treatment (12,13).

Despite the progress in pre-surgical instrumental exami-
nations (head and neck CT scan, neck echo-color Doppler,
fibrolaryngoscopy, esophageal-gastric-duodenoscopy,
bronchoscopy and PET), clinical lymph node staging is not
completely error-free due to false positivity in the presence of
reactive lymph nodes, non metastatic lymph node enlargement
and false negativity for small- or micrometastases clinically
undetectable (14,15). Finally, the controversial role of sentinel
lymph node positivity and the surgical morbidity after ND
have led to the evaluation of alternative and super-selective
surgeries in order to reduce the overtreatments (15,16-18).

For these reasons, further in-depth studies regarding the
behaviour of lymph node cervical metastases may be useful
to refine therapeutic management, thereby decreasing the
overtreatment-related morbidity and mortality.

The aim of the present study was to define LNM frequency,
topographic distribution, size (micrometastases vs. macrome-
tastases) and histological pattern correlating them with the
clinical features of primary tumour in 121 OSCC patients who
had undergone ND, considering the survivals related to their
presence/absence and the morbidity related to the negative ND
and due to the neck surgery, comparing our results with the
literature and suggesting an evidence-based re-evaluation of
the therapeutic approach to ND.

Materials and methods

Study population and clinical pathological data. Resection
specimens from 121 patients who had undergone ND
surgery for OSCC at the National Cancer Institute of Naples,
‘G. Pascale’, Italy, between the years 1993-2004, formed
the basis of the present retrospective analysis. All patients
underwent MRND for OSCC (11,19). Patients who had had
previous surgery (other than diagnostic biopsy) were excluded.
Throughout the time period of the study, the resection spec-
imens were performed by the same surgical team and were
assessed by the same pathological team. Pathological report
and topography of the extent and location of the metastatic
disease for each patient were reviewed and number, size
and histological patterns of LNM-positive cases (pN+) were
re-evaluated according to previous literature (14,15,20,21) in
order to calculate frequency, distribution and other significant
statistical correlations existing between primary tumour
features and pN+.

The series comprised 80 males (mean age of 63.10±10.79
years; range, 30-83 years, median 63 years) and 41 females
(mean age, 63.12 ±51.9; range, 25-86 years, median,
65 years). The cTaN staging was assessed according to the
6th edition AJCC (2) since data refer to the period between
1999-2004. Patient demographic and clinical characteristics
of the 121 cases are summarized in Table I.

Pre-operative, operative and post-operative protocols. At the
National Cancer Institute of Naples ‘G. Pascale’, Italy, the selec-
tion of OSCC cases requiring ND depends on the cTaN (2).
cTaN parameters are accurately quantified after performing a
series of clinical-instrumental examinations such as PET, total
body CT scan, neck echo-color Doppler, fibrolaryngoscopy,
esophageal-gastric-duodenoscopy, bronchoscopy and, if any
doubts persist, fine needle aspiration biopsy (FNAB) and
biopsy.

According to the literature, MRNDs are considered
mandatory for the OSCCs clinically showing cervical LNMss
(any cT/N+ and therapeutic ND), for locally advanced primary
tumours with clinically undetectable LNMss (cT3/N0 and cT4/
cN0, elective ND) and in the cases of small primary tumours
clinically negative to node involvement (cT1-T2/N0) that
during intraoperative assessment of their sentinel lymph node
reveal a positivity to metastasis (SLN+) (8,9).

For the ND surgical approach, we adopted MRND (10), thus
involving levels I-IV for all oral sub-sites, except for trigone,
posterior tongue and anterior pillar where ND extended until
level V; level IIB was always comprised.

After surgery and histopathological assessment of the
margins of excision of the primary tumour and after the
evaluation of the involvement of the surroundings structures,
adjuvant therapy was performed; radiotherapy for T4 tumours
with free-surgical margins and/or ≥N2, and both radiotherapy and chemotherapy both for tumours with any N+ plus ECS, tumours with any T and positive or close margins or perineural invasion and/or neoplastic vascular embolization tumours T1-3 with free margins and pN0/pN1 were not enrolled for adjuvant treatments (12,13).

Since data refer to patients recruited from 1999 to 2004, prior to the last Cancer Staging Atlas publication, we consid-
ered the previous edition (2); hence, T4 tumours were not
distinguished in T4a and T4b, consequently, stage IV has not
been subclassified into stages IVa, IVb and IVc (7).

Histopathological node metastasis classification. All 121
lymph node specimens dissected were histopathologically
re-evaluated for the present study. In order to detect microme-
tastases and to confirm the involvement of lymph nodes, the
standardized sectioning protocol was performed. One H&E
stained section was prepared from each block and examined
for the presence of nodal involvement by tumour. If present,
 metastatic disease was reported. If node was negative or
equivocal for metastatic disease, or positive for micrometas-
tases, the removed lymph nodes were also serially sectioned
at 25-µm intervals 4 µm thick and alternately stained with
H&E and immunohistochemical staining (IHC) using anti-
cytokeratin and EMA antibodies (Fig. 1) as described below.
This pattern was continued throughout the entire block. Each
immunostained component was always compared with adja-
cent sections stained by H&E.

Woolgar’s classification criteria were considered in order
to classify the type of metastasis (21,22). Woolgar distin-
guished metastatic lymph nodes into two groups with different
prognosis and features: typical metastatic pattern as ‘orderly
involvement of successive anatomical nodal levels, creating an
inverted cone with maximum volume and maximum ECS at
levels I or II and a gradual reduction in the volume/extent of
metastasis at the numerically higher levels’ (21), vs. atypical
metastatic pattern, termed ‘aberrant’ by Woolgar, and
characterized by various features. The ones referring to the
atypical pattern and considered in the present study were the
involvement of ‘other’ anatomical groups of nodes (including
parapharyngeal, facial, buccal, lingual and sublingual nodes),
involvement of contralateral cervical lymph nodes, skipping of
anatomical levels other than level I and the presence of a single
micrometastasis (21).

Once defined, the histopathological features of node metas-
tases were correlated with the clinical and histopathological
features of the primary tumour in order to establish statistical
and prognostic correlations.

Immunohistochemistry. Histological and immunohis-
tochemical analyses were performed on formalin-fixed,
paraffin-embedded tissue samples. Immunostaining was
performed using the linked streptavidin-biotin horseradish
peroxidase technique (LSAB-HRP). Antigen retrieval was
performed by microwave heating, a first time for 3 min at
650 W, a second and a third time for 3 min at 350 W, the slides
immersed in 10 mM citrate buffer pH 6.0. After heating, the
sections were blocked for 60 min with 1.5% horse serum
(Santa Cruz Biotechnology) diluted in PBS buffer before
reaction with the primary antibody (Ab). The primary mono-
oclonal antibodies anti CK AE1/AE3 (dilution 1:50, pH  6.0;
Dako, Carpinteria, CA, USA) and EMA (dilution 1:75, with
protein K; Dako) were incubated overnight. After two washes

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Table I. Patient demographics and clinical characteristics.

<table>
<thead>
<tr>
<th></th>
<th>N (%)</th>
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<tbody>
<tr>
<td>Gender (male/female)</td>
<td>80/41 (66/34)</td>
</tr>
<tr>
<td>Male mean age, years</td>
<td>63.10 (30-83)</td>
</tr>
<tr>
<td>Female mean age, years</td>
<td>63.12 (25-86)</td>
</tr>
<tr>
<td>Primary T site</td>
<td></td>
</tr>
<tr>
<td>Tongue</td>
<td>53 (44)</td>
</tr>
<tr>
<td>Floor of the mouth</td>
<td>23 (19)</td>
</tr>
<tr>
<td>Cheek</td>
<td>4 (3)</td>
</tr>
<tr>
<td>Trigone</td>
<td>17 (14)</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>8 (7)</td>
</tr>
<tr>
<td>Palate</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Fornix</td>
<td>10 (9)</td>
</tr>
<tr>
<td>Not specified</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Histologic grade</td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>35 (29)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>65 (54)</td>
</tr>
<tr>
<td>High</td>
<td>21 (17)</td>
</tr>
<tr>
<td>AJCC stage</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>11 (9)</td>
</tr>
<tr>
<td>II</td>
<td>30 (25)</td>
</tr>
<tr>
<td>III</td>
<td>28 (23)</td>
</tr>
<tr>
<td>IV</td>
<td>52 (43)</td>
</tr>
</tbody>
</table>

Figure 1. Immunohistochemical H&E staining of a node metastasis showing
cytokeratin and EMA positivity confirming the presence of OSCC metas-
tases in the lymph nodes evaluated.
with PBS, the slides were treated with biotinylated species-specific secondary antibodies and streptavidin-biotin enzyme reagent (Dako, Glostrup, Denmark), and the colour developed by 3,3’-diaminobenzidine tetrahydrochloride. Sections were counterstained with Mayer’s hematoxylin and mounted using xylene-based mounting medium. In negative controls, the primary antibody was omitted. The results of the IHC were separately evaluated by two independent observers by carefully examining the entire section with an optical microscope (Olympus BX41). For each case, the presence and the extent of positive cells in all sections examined was determined. Isolated tumour cells (ITCs) are defined as tumour cell clusters that are not >0.2 mm in largest diameter and are denoted as lymph node negative (pN0i+). Micrometastases are defined as metastases that are >0.2 mm in diameter but ≤2 mm, denoted as lymph node positive (pN1mi). Carcinoma macrometastases measured >2 mm in maximum extent. Two investigators experienced in oral pathology blindly and independently examined the study sections initially, and then they evaluated together the histopathological and immunostained sections until they reached an agreement.

**Statistical analysis.** Data were analysed by the GraphPad Prism software version 5.0 for Windows (GraphPad Software, San Diego, CA, USA; www.graphpad.com) and Excel Microsoft Office. Differences among the groups were estimated using the one-way analysis of variance (ANOVA) and the Student-Newman-Keuls test. Only P-values <0.05 were considered significant. Overall survivals in the different groups were calculated by the Kaplan-Meier curves and log-rank (Mantel-Cox) test was applied for comparing survival probabilities. The pathological positivity of the ND (pN+) and the type of LNMs were correlated with the site of primary tumour. The percentages of positive node metastases (pN+) in elective, therapeutic and secondary to SLN+ NDs and the number of lymph nodes harvested were also evaluated.

**Results**

**Differentiation degree, cTNM staging and pN status of 121 cases.** Patient demographics and characteristics such as gender, OSCC site, primary tumour differentiation grading and cTNM staging according to the international guidelines (2) of the 121 OSCCs considered are shown in Table I.

At pre-surgical clinical-instrumental evaluation, 61/121 cases (50.4%) were considered positive (cN+) and 60/121 (49.6%) negative (cN0) to node metastases. The histopathological lymph node assessment subsequent to ND revealed at least one node metastasis in 56/121 NDs, thus considered pathologically positive lymph nodes (pN+) and no node metastasis in the remaining 65 cases, which were considered pathologically negative lymph nodes (pN0). The percentages of true positive (cN+ and pN+), true negative (cN0 and pN0), false positive (cN+ and pN0) and false negative (cN0 and pN+) were 87, 95, 13 and 5% respectively, as reported with details of accuracy, sensitivity, specificity, and positive and negative predictive values in Fig. 2.

The pN+ distribution according to the grading, staging MRND intent and, conversely, the pN+ frequency in each group are reported in Table II.

**Distribution of 121 MRNDs according to intent to surgery and related pN+ frequencies.** Among the 121 NDs considered, 61/121 (50%), presenting at least a clinical node involvement (cN+), were therapeutic NDs; 19/121 (16%), presenting a cT3/cT4 and cN0 were elective NDs; the remaining 41/121 (34%), presenting primary tumours small in size (cT1/cT2) and no evident clinical node metastases (cN0) but positive to sentinel lymph node metastases (SLN+) during the intraoperative assessment of sentinel lymph node, were NDs performed to establish the presence of other node metastases in addition to SLN+ (Table II). The distribution of 56 pN+ according to clinical-instrumental indications and, conversely, the pN+ frequency in each indication are reported in Table II.

**pN+ pattern.** After excluding 19 pN+ cases due to lack of data useful to classify the pN+ histopathological pattern, the remaining 37 pN+ NDs were distinguished into 17/37 with typical (46%) and 20/37 with atypical (54%) node metastases according to Woolgar’s classification (21). The atypical pattern was largely represented by skip metastases [10/20 (50%)], followed by the frequency of bilateral metastases [5/20 (25%)], micrometastases [2/20 (10%)], involvement of other lymph nodes alone [2/20 (10%)], and 1/20 (5%) showing both micrometastases and other lymph nodes co-interested (Fig. 3A). According to primary tumour site, skip metastases indiscriminately involved any site of the oral cavity, except cheek and fornx, which, on the contrary, preferentially showed micrometastases; bilateral metastases were frequently detected in OSCCs affecting tongue as a single site or in association with floor of the mouth or trigone; ‘other different lymph nodes’ were involved in floor of the mouth tumours (Fig. 3B and C).

Among 56 pN+ cases, 15/56 pN+ (26.8%) involved levels I-III, 11/56 pN+ (19.6%) involved levels IV-V, and 30/56 (53.6%) pN+ were censored due to level not reported.

ND anatomical levels I-III were typically involved by node metastases while levels IV-V showed pN+ only for primary tumours of trigone, floor of the mouth plus tongue, tongue alone and multiple sites (data not shown).

**Number of lymph nodes removed.** A total of 3,390 lymph nodes were harvested in 121 NDs, mean 18.5±22.7 per ND, range 1-110. One hundred and sixty-two lymph nodes were harvested in 121 NDs, mean 18.5±22.7 per ND, range 1-110.
Recurrence. Recurrence was observed in 8 cases, whose clinical, histological and lymph node features are shown in Table III.

Survival curves. Overall survival statistical significance and percentages of subjects alive at 1, 2 and 5 years from the diagnosis are reported in Table IV.

Table II. pN+ distribution and frequency according to histological grading, AJCC staging and MRND intent.

<table>
<thead>
<tr>
<th>Histological grade</th>
<th>Total ND cases (%)</th>
<th>pN+ distribution according to grade</th>
<th>Total pN+ cases in each group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>35 (29)</td>
<td>11/56 (20)</td>
<td>11/35 (31)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>65 (54)</td>
<td>32/56 (57)</td>
<td>32/65 (49)</td>
</tr>
<tr>
<td>High</td>
<td>21 (17)</td>
<td>13/56 (23)</td>
<td>13/21 (62)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>cTNM</th>
<th>Total ND cases (%)</th>
<th>pN+ distribution according to cTNM</th>
<th>Total pN+ cases in each group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>11 (9)</td>
<td>0/56 (0)</td>
<td>0/11 (0)</td>
</tr>
<tr>
<td>Stage II</td>
<td>30 (25)</td>
<td>2/56 (4)</td>
<td>2/30 (6.6)</td>
</tr>
<tr>
<td>Stage III</td>
<td>28 (23)</td>
<td>13/56 (23)</td>
<td>13/28 (46.4)</td>
</tr>
<tr>
<td>Stage IV</td>
<td>52 (43)</td>
<td>41/56 (73)</td>
<td>41/52 (79)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>cT status</th>
<th>cN status</th>
<th>MRND clinically accorded</th>
<th>Total ND cases (%)</th>
<th>pN+ according to MRND intent</th>
<th>Total pN+ cases in each group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any T</td>
<td>cN+</td>
<td>Therapeutic</td>
<td>61/121 (50)</td>
<td>53/56 (94)</td>
<td>53/61 (88.3)</td>
</tr>
<tr>
<td>T3 or T4</td>
<td>cN0</td>
<td>Elective</td>
<td>19/121 (16)</td>
<td>1/56 (2)</td>
<td>1/19 (5.3)</td>
</tr>
<tr>
<td>T1 or T2</td>
<td>cN0</td>
<td>Secondary to SLN+</td>
<td>41/121 (34)</td>
<td>2/56 (4)</td>
<td>2/42 (4.8)</td>
</tr>
</tbody>
</table>

Figure 3. Atypical metastatic pattern frequencies (A) and their distributions (B and C) according to primary tumour site. (C) Distribution of the 19 pN+ atypical metastases according to pattern and primary tumour site. The case showing both micrometastases and other lymph nodes co-interested has not been included. Ln, lymph node; T, tongue; PIL, pillars; F, fornix; FOM, floor of the mouth; TR, trigone; C, cheek.

Overall survival was statistically different according to early AJCC vs. late AJCC stages (P=0.0004) with a 5-year survival of 78.34 and 46.16%, respectively, and according to absence/presence of nodal metastases (pN0 vs. pN+, P=0.0003) with a 1-5 year overall survival ranging between 97-74% in pN0 cases and between 69-54% in pN+ cases.
Despite these findings, statistically significant differences in advanced staging, the more frequent the nodal metastases. The primitive tumour was towards undifferentiation and AJCC partly in accordance with previous literature (23).

In an attempt to identify a better prognosis. Our results are metastasis (LNM) has been reported by several investigators of histological differentiation and the incidence of lymph node different studies and a close relationship between the degree staging, recurrence and prognosis have been published in OS the remaining 94.7 and 95.2% of cases, respectively. pN+ was found in 2 out of 42 NDs performed after SLN+ (0/11, 0%, pN+ in cT1-cN0M0 NDs and 2/31, 6.45%, in cT2-cN0M0 NDs), thus confuting previous literature supporting its role as a diagnostic marker for other nodal metastases (24,25) and bringing the predictive role of SLN positivity into discussion, leading us to conclude that a ND secondary to SLN+ is an overtreatment in 100% of cT1-cN0M0 NDs and in 93.55% of cT2-cN0M0 NDs. We suggest conducting further biomolecular studies focusing on molecular markers able to predict occult metastatic disease in SLN biopsies, thereby improving the quality of the treatments (26).

The significant association between clinical staging and histopathological report, confirmed by high accuracy (90.9%) revealed the quality of the pre-surgical clinical and instrumental staging of the tumours.

With regard to the anatomical lymph nodal levels involved, results showing involvement of levels IV-V only for primary tumours of trigone, floor of the mouth plus tongue, tongue alone and multiple sites, express the major morbidity of the OSCCs of these primary sites, requesting an ND extended until level V and lead us to re-consider the extended ND in the cases of OSCC affecting different oral sites such as cheek, which never showed levels of IV-V involvement in the present study. Shah (27) provided evidence that the pattern of neck metastasis of carcinomas from upper aerodigestive tract is predictable based on the location of the primary lesion. Moreover, it has been shown that in patients with oral carcinoma and clinical evidence of neck disease, the rate of pathologic involvement of level V nodes was only 4%. In the present study, the percentage of pathologic involvement of level IV-V nodes was 19.6%, higher when compared with the 4% value reported by Shah (27).

Recurrences, observed in 8 cases, mainly occurred in floor of the mouth and tongue OSCCs, at intermediate grade of differentiation and independently from the pN status.

The survival probability was in accordance with the number of lymph nodes harvested, as previously demonstrated by Amar et al (6), who found the larger number of lymph nodes overall survival were observed only in relation to AJCC staging and not according to histological grading.

Since 88.3% of NDs performed for therapeutic intent presented at least one pN+, the therapeutic value was confirmed. On the contrary, the low pN+ frequencies in elective NDs (5.3%) and in NDs secondary to SLN+ (4.8%) revealed an overtreatment in cases, respectively. pN+ was found in 2 out of 42 NDs performed after SLN+ (0/11, 0%, pN+ in cT1-cN0M0 NDs and 2/31, 6.45%, in cT2-cN0M0 NDs), thus confuting previous literature supporting its role as a diagnostic marker for other nodal metastases (24,25) and bringing the predictive role of SLN positivity into discussion, leading us to conclude that a ND secondary to SLN+ is an overtreatment in 100% of cT1-cN0M0 NDs and in 93.55% of cT2-cN0M0 NDs. We suggest conducting further biomolecular studies focusing on molecular markers able to predict occult metastatic disease in SLN biopsies, thereby improving the quality of the treatments (26).

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Correlation among histological malignancy grading in OSCC and different clinical parameters such as clinical staging, recurrence and prognosis have been published in different studies and a close relationship between the degree of histological differentiation and the incidence of lymph node metastasis (LNM) has been reported by several investigators in an attempt to identify a better prognosis. Our results are partly in accordance with previous literature (23).

Descriptive data showed, as expected, that the more the primitive tumour was towards undifferentiation and AJCC advanced staging, the more frequent the nodal metastases. Despite these findings, statistically significant differences in

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### Table III. Clinical, histological and lymph node features in the 8 cases with recurrence.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age (years)</th>
<th>T site</th>
<th>Histological grade</th>
<th>AJCC stage</th>
<th>pN status</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>80</td>
<td>FOM</td>
<td>Low</td>
<td>II</td>
<td>pN0</td>
<td>Alive</td>
</tr>
<tr>
<td>Female</td>
<td>83</td>
<td>FOM</td>
<td>Intermediate</td>
<td>III</td>
<td>pN+</td>
<td>Alive</td>
</tr>
<tr>
<td>Female</td>
<td>48</td>
<td>Tongue</td>
<td>Intermediate</td>
<td>IV</td>
<td>pN+</td>
<td>Alive</td>
</tr>
<tr>
<td>Female</td>
<td>70</td>
<td>Tongue</td>
<td>Low</td>
<td>I</td>
<td>pN0</td>
<td>Deceased</td>
</tr>
<tr>
<td>Male</td>
<td>64</td>
<td>Tongue</td>
<td>Intermediate</td>
<td>II</td>
<td>pN0</td>
<td>Deceased</td>
</tr>
<tr>
<td>Male</td>
<td>57</td>
<td>FOM, Tongue</td>
<td>Intermediate</td>
<td>IV</td>
<td>pN+</td>
<td>Alive</td>
</tr>
<tr>
<td>Male</td>
<td>70</td>
<td>Fornix</td>
<td>Intermediate</td>
<td>III</td>
<td>pN+</td>
<td>Deceased</td>
</tr>
<tr>
<td>Male</td>
<td>76</td>
<td>Trigone</td>
<td>Intermediate</td>
<td>IV</td>
<td>pN0</td>
<td>Deceased</td>
</tr>
</tbody>
</table>

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**Discussion**

In the present study, a descriptive and statistical retrospective study on 121 OSCCs who had undergone neck dissection (ND) was conducted, focusing on metastatic pattern (typical vs. atypical), number of lymph nodes harvested and node metastasis features in terms of size, anatomical extent and surgical decision orienting the ND (elective, therapeutic and after SLN+).

Correlation among histological malignancy grading in OSCC and different clinical parameters such as clinical staging, recurrence and prognosis have been published in different studies and a close relationship between the degree of histological differentiation and the incidence of lymph node metastasis (LNM) has been reported by several investigators in an attempt to identify a better prognosis. Our results are partly in accordance with previous literature (23).

Descriptive data showed, as expected, that the more the primitive tumour was towards undifferentiation and AJCC advanced staging, the more frequent the nodal metastases. Despite these findings, statistically significant differences in
dissected in the ND related to the group of better prognoses among pN0 cases, while we found this result independently from the pN status.

We also confirmed the statistically significant different survival probability of patients with micrometastases (5-year, 40%), intermediate among pN0 (5-year, 69.10%) and pN+ with macrometastases patients (5-year, 28.68%), as previously reported by Broglie et al. (20) and Han et al. (28).

Statistically significant difference in the overall survival was also found according to clinical intent to surgery independently from the pN0, with a better prognosis in patients who had undergone elective ND or after SLN+ when compared with the ones who had undergone therapeutic ND, independently from pN status.

In conclusion, the surgical management of regional metastatic neck disease in patients with oral and oropharyngeal

<table>
<thead>
<tr>
<th>Table IV. One-, 2- and 5-year overall survival and the statistical significance.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Stage I-II</td>
</tr>
<tr>
<td>Stage III-IV</td>
</tr>
<tr>
<td>Low grade</td>
</tr>
<tr>
<td>Intermediate-high grade</td>
</tr>
<tr>
<td>pN0</td>
</tr>
<tr>
<td>pN+</td>
</tr>
<tr>
<td>pN+/Stage I-II</td>
</tr>
<tr>
<td>pN+/Stage III-IV</td>
</tr>
<tr>
<td>pN+/Low grade</td>
</tr>
<tr>
<td>pN+/Intermediate-high grade</td>
</tr>
<tr>
<td>Typical pN+</td>
</tr>
<tr>
<td>Atypical pN+</td>
</tr>
<tr>
<td>Typical pN+/Low grade</td>
</tr>
<tr>
<td>Typical pN+/Intermediate-high grade</td>
</tr>
<tr>
<td>Atypical pN+/Low grade</td>
</tr>
<tr>
<td>Atypical pN+/Intermediate-high grade</td>
</tr>
<tr>
<td>pN+ with ECS/macrometastases</td>
</tr>
<tr>
<td>pN+ with micrometastases</td>
</tr>
<tr>
<td>pN0</td>
</tr>
<tr>
<td>LN&lt;20</td>
</tr>
<tr>
<td>LN 20-30</td>
</tr>
<tr>
<td>LN&gt;30</td>
</tr>
<tr>
<td>pN0/Elective</td>
</tr>
<tr>
<td>pN0/Therapeutic</td>
</tr>
<tr>
<td>pN0/SLN+</td>
</tr>
<tr>
<td>pN+/Elective</td>
</tr>
<tr>
<td>pN+/Therapeutic</td>
</tr>
<tr>
<td>pN+/SLN+</td>
</tr>
<tr>
<td>SLN+</td>
</tr>
<tr>
<td>E</td>
</tr>
<tr>
<td>T</td>
</tr>
<tr>
<td>pN+/SLN+</td>
</tr>
<tr>
<td>pN+/E</td>
</tr>
<tr>
<td>pN+/T</td>
</tr>
<tr>
<td>pN0/SLN+</td>
</tr>
<tr>
<td>pN0/E</td>
</tr>
<tr>
<td>pN0/T</td>
</tr>
</tbody>
</table>

*pThere were 2 pN+/Stage I-II subjects. *The 2 patients pN+/SLN+ died after 9 months.
cancer remains a topic of debate and controversy. For several years classical comprehensive ND has been the mainstay of treatment. Selective and super-selective neck treatments were recently introduced and widely applied in order to reduce morbidity and mortality related to extensive ND, thus improving the postoperative quality of life after preservation of level V and the surrounding anatomical structures.

With regard to atypical metastases according to Woolgar’s definitions, no statistically significant differences were found related to the overall survival of this group vs. typical metastatic pattern. However, we noted different atypical features related to different primary tumour sites. Our data suggest that enhancing our knowledge of these types of atypical patterns site-related, and further evaluations such as novel imaging techniques (29) and molecular analyses (30) may help us to understand if any behaviour and biomolecular differences exist among OSCCs according to site.

References