

Watchful waiting of the neck in early stage oral cancer is unfavourable for patients with occult nodal disease

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Abstract. For cT1/2N0 oral squamous cell carcinoma (OSCC), treatment of the neck is a matter of debate. Two treatment strategies were evaluated in this study: selective neck dissection (SND) and watchful waiting (WW). One hundred and twenty-three SND patients and 70 WW patients with cT1/T2N0M0 OSCC of the tongue, floor of mouth, or buccal mucosa were analysed retrospectively. Extracapsular spread (ECS), 3-year overall survival (OS), and disease-specific survival (DSS) were determined. Twenty-nine percent of SND patients and 13% of WW patients had occult nodal disease. WW-N+ patients showed thicker tumours as compared to WW-N0 patients (5 mm vs. 2 mm, $P = 0.02$). WW-N+ patients showed significantly more ECS as compared to SND-N+ patients (56% vs. 14%, $P = 0.016$) and had a significantly worse 3-year DSS than SND-N+ patients (56% vs. 82%, $P = 0.02$). For T1 OSCCs, a watchful waiting policy is acceptable if tumour thickness proves to be <4 mm. Otherwise, an additional treatment of the neck is advised, since WW-N+ patients show more ECS, with a worse DSS than SND-N+ patients.

Key words: oral squamous cell carcinoma; selective neck dissection; watchful waiting; metastasis; extracapsular spread.

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For most patients with early stage (T1/T2N0) oral squamous cell carcinoma (OSCC), the preferred treatment is surgical excision of the primary tumour. The management of the clinically negative neck (cN0) remains a matter of debate.^{1–6} The intervention and related side effects of a selective neck dissection

(SND) or elective radiation therapy must be weighed against the benefits of possibly better regional control. About 20–40% of early stage OSCC patients have occult nodal disease in the neck.^{3,5,7,8} Despite imaging, such as magnetic resonance imaging (MRI), computed tomography (CT), and ultrasonography (US), and even fine

needle aspiration cytology (FNAC), a substantial proportion of these metastases remain undetected.^{4,9,10}

Gene or protein expression profiling of the primary tumour, which may have additional value for the identification of tumours with a high propensity for early metastatic spread,^{7,11} is not yet applied

routinely.⁷ Also the sentinel node biopsy for OSCC has still not gained wide acceptance. The decision whether or not to treat the cN0 neck is therefore often based on a combination of clinicopathological tumour characteristics, imaging, and FNAC.^{3,4,8,12} Consequently, patients with a true pN0 neck may receive an unnecessary SND with the risk of perioperative and postoperative complications.^{13,14} Alternatively, proper treatment may be withheld from patients with a true pN+ neck, and these patients may be confronted with lymph node metastases during follow-up, sometimes even with extracapsular spread (ECS). Some studies report that a 'watchful waiting' (WW) policy can be accepted for small oral cancers.^{15,16}

The aim of this retrospective study was to evaluate the current treatment strategy of the cN0 neck in stage I–II OSCC at the authors' institution. This strategy consists of a SND for cT1–T2N0M0 OSCCs and watchful waiting in the case of cT1N0M0 OSCCs with a diameter of <15 mm and thickness of <5 mm. The distribution of occult metastases, the incidence of ECS, and survival rates were analysed.

Patients and methods

Patients

A retrospective chart review was conducted of 226 consecutive patients with pT1–2 cN0 OSCC of the tongue, floor of the mouth, or buccal mucosa (International Classification of Diseases for Oncology 3rd edition (ICD-O-3) locations C02.0–C02.3, C04, and C06.0), who were treated with a primary surgical resection between 2004 and 2010. Thirty-three patients were excluded: 21 because of a previous head and neck malignancy, two because a sentinel node biopsy was performed, three because they had received primary radiotherapy of the neck, and seven because a SND was indicated (see below) but not done due to co-morbidity. Staging was performed in accordance with the 2002 Union for International Cancer Control (UICC) criteria. Pertinent data are listed in Table 1.

Methods

CT or MRI was performed for OSCCs staged as cT2 and cT1 with a clinically estimated infiltration depth of ≥ 5 mm. US of the neck was performed with FNAC when a node showed a short transverse diameter > 5 mm, an abnormal shape, or a deviant architecture. A SND was performed in all patients with a suspicion

Table 1. Clinicopathological characteristics of cN0 patients according to the type of treatment.

Characteristics	SND (n = 123)	WW (n = 70)	P-value
Sex, n (%)			0.14 ^a
Male	75 (61)	35 (50)	
Female	48 (39)	35 (50)	
Age (years)			0.25 ^b
Mean (SD)	62 (11)	64 (15)	
Range	35–86	23–90	
ECOG score, n (%)			0.10 ^c
0	87 (78)	39 (65)	
1	18 (16)	12 (20)	
≥ 2	6 (5)	9 (15)	
Smoking, n (%)			0.06 ^a
Yes	68 (55)	29 (41)	
No	55 (45)	41 (59)	
Alcohol, n (%)			0.94 ^a
Yes	71 (58)	40 (57)	
No	52 (42)	30 (43)	
Primary tumour site, n (%)			0.28 ^a
Tongue	67 (55)	32 (46)	
Floor of mouth	42 (34)	32 (46)	
Cheek	14 (11)	6 (9)	
Tumour diameter (mm)			<0.001 ^d
Median	20.0	7.5	
IQR	13.5–26.5	3.5–11.5	
Tumour thickness (mm)			<0.001 ^d
Median	7.0	2.0	
IQR	3.0–11.0	1.0–3.0	
Growth pattern, n (%)			0.02 ^a
Infiltrative	84 (68)	36 (51)	
Perineural	42 (34)	5 (7)	<0.001 ^c
Vascular invasive	14 (11)	0 (0)	0.002 ^c

ECOG, Eastern Cooperative Oncology Group; IQR, interquartile range; SD, standard deviation; SND, selective neck dissection; WW, watchful waiting.

^a Pearson's χ^2 test.

^b Unpaired *t*-test.

^c Fisher's exact test.

^d Mann–Whitney *U*-test.

of nodal disease on US, not confirmed by FNAC, or an estimated infiltration depth of more than 5 mm.

Patients were assigned to a WW policy for cT1 tumours with both a clinical diameter < 15 mm and an estimated infiltration depth < 5 mm, and if no nodal disease was suspected on imaging or FNAC. The surgical intervention consisted of wide transoral excision of the tumour (10-mm macroscopic margins), with or without an intentional SND level I–III, performed by one of four surgeons specialized in head and neck surgical oncology.

SND patients underwent surgical resection of the primary tumour combined with an intentional SND level I–III, not necessarily en bloc. During the operation, frozen sections were made for the histopathological examination of suspicious lymph nodes. In the case of metastasis, a modified radical neck dissection was performed in the same procedure.

WW patients underwent surgical resection of the primary tumour without treatment of the neck. US examination was intended every 3–4 months in the first

postoperative year, or in the case of palpable nodes. The development of regional metastases and the distribution over different subgroups was analysed. All patients were followed-up for at least 3 years.

Within these two groups, two subgroups were identified: (1) SND-N+ patients, who were patients with occult nodal metastasis in the SND group, i.e. patients in the SND group with either a pathological positive neck (pN+) or with a pathological negative neck (pN0) who developed regional metastasis without local recurrence during follow-up, and (2) WW-N+ patients, who were patients with occult nodal metastasis in the WW group, i.e. patients in the WW group who developed regional metastasis without local recurrence during follow-up.

Figure 1 shows the total cohort and the different subgroups.

Histological analysis

A dedicated head and neck pathologist (SMW) assessed the surgical resection specimens of the primary tumour and

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