



Elective neck dissection in unilateral carcinomas of the tongue: Unilateral versus bilateral approach



Christopher-Philipp Nobis^{a,*}, Sven Otto^{b,1}, Tamara Grigorieva^b, Mohamed Alnaqbi^b, Matthias Troeltzsch^b, Jakob Schöpe^c, Stefan Wagenpfeil^c, Michael Ehrenfeld^b, Klaus-Dietrich Wolff^a, Marco Rainer Kesting^a

^a Department of Oral and Maxillofacial Surgery, Klinikum rechts der Isar, Technische Universität München, Ismaninger Str. 22, D-81675 Munich, Germany

^b Department of Oral and Maxillofacial Surgery, Ludwig-Maximilians-Universität München, Lindwurmstraße 2a, D-80337 Munich, Germany

^c Institute for Medical Biometry, Epidemiology and Medical Informatics, Universität des Saarlandes, Homburg/Saar, Germany

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ABSTRACT

Purpose: Elective neck dissection (END) is a common primary treatment strategy for oral tongue squamous cell carcinoma (OTSCC), although uncertainty remains regarding the necessary extent of END for strictly unilateral early stage OTSCC. The authors evaluated two END variations, unilateral and bilateral, to determine the optimal extent.

Materials and methods: A retrospective cohort study was performed on patient data from two departments of oral and maxillofacial surgery. All previously untreated patients from both clinics who were diagnosed with early-stage (pT1-2) unilateral OTSCC were included. The following variables were collected: age, gender, END type/extent, tumor localization, later nodal metastasis, and TNM status. Statistical analyses were performed ($p < 0.05$).

Results: A total of 150 patients were identified, 105 receiving unilateral END and 45 bilateral END. The rates of postoperative positive lymph nodes were 21.9% for ipsilateral END and 26.7% for bilateral END (bilateral END: all positive nodes ipsilateral). In all, 14 patients in the ipsilateral group developed nodal metastasis during tumor aftercare (11 patients ipsilateral, 3 patients contralateral neck). In the bilateral group, nodal metastasis was later observed in 4 cases (8.9%; 3 cases ipsilateral, 1 case contralateral neck). Statistical analysis could not detect significant differences between the END procedures.

Conclusion: As both procedures lead to similar results in preventing or omitting possible later nodal metastasis, the two methods seem to be valuable alternatives. In conclusion, we recommend bilateral END because of advantages with regard to oncologic safety and esthetic outcome, but the decision for END should always be according to the patient's general health status, comorbidities, and individual tumor risk profile.

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1. Introduction

The tongue is the most frequent location with regard to oral cancer (Moore et al., 2000). In general, malignancies of the oral cavity are the seventh most common tumors in German males. Incidence rates of 17.9 per 100,000 for males and 6.0 per 100,000 for females in Germany make it a serious health threat (Robert Koch Institut, 2015). Concerning the tongue, the estimated male incidence rates per year show a large amount of variation, e.g., from 9.4 in India to 1.1 in the UK (Moore et al., 2000; Prince and Bailey, 1999). Over 95% of these malignancies are squamous cell carcinomas, associated with the classic risk factors of alcohol and tobacco, and a

* Corresponding author. Department of Oral and Maxillofacial Surgery, Technische Universität München, Klinikum Rechts der Isar, Ismaninger Str. 22, 81675 Munich, Germany.

E-mail addresses: christopher-nobis@t-online.de (C.-P. Nobis), sven.otto@med.uni-muenchen.de (S. Otto), tamara.grigorieva@web.de (T. Grigorieva), mohamed.alnaqbi@med.uni-muenchen.de (M. Alnaqbi), matthias.troeltzsch@med.uni-muenchen.de (M. Troeltzsch), schoepe@med-imbei.uni-saarland.de (J. Schöpe), sw@med-imbei.uni-saarland.de (S. Wagenpfeil), michael.ehrenfeld@med.uni-muenchen.de (M. Ehrenfeld), wolff@mkg.med.tum.de (K.-D. Wolff), marco.kesting@tum.de (M.R. Kesting).

¹ Contributed equally to this study and should be considered as co-first authors.

combination of these two factors seems to multiply the tumor development risk (Talamini et al., 2002). At the molecular level, an overexpression of vascular endothelial growth factor (VEGF) and its isoforms (Aggarwal et al., 2014; Kyzas et al., 2005) and of VEGF receptors (Pianka et al., 2015) is commonly observed in oral squamous cell carcinomas (OSCC). Primary treatment of oral tongue squamous cell carcinomas (OTSCC) usually involves resection of the tumor lesion (Wolff et al., 2012). To address, in oral cancer, the high rates of occult metastasis, which show a high amount of variation throughout the literature with ranges of up to 34% (Dogan et al., 2014; Shah et al., 1990), subsequent neck dissection to a variable extent is performed according to the patient's estimated risk profile. Therefore, an elective neck dissection of the ipsilateral levels I–III in all affected patients is recommended as oral cavity carcinoma treatment (Wolff et al., 2012). Based on the final histopathological findings, recommendations for postoperative therapy can be given. These can include radiotherapy or, in cases of extracapsular lymph nodes, a combination of radio- and chemotherapy. Although many advances regarding operative and postoperative treatment have been made during the past few decades, the absolute 5-year survival rate in Germany averages about 50% (males: 43%; females: 55%) (Robert Koch Institut, 2015). This poor rate is mainly caused by metastatic disease at regional or distant sites and by local recurrence (Sano and Myers, 2007; Yuen et al., 1997). The literature is consistent in showing that the most reliable prognostic factor in OTSCC is the presence of cervical metastasis in the lymph nodes (Grandi et al., 1985; Sano and Myers, 2007; Schuller et al., 1980). Because of the above-mentioned poor survival rates, the effective treatment of OTSCC remains challenging. In consequence, a sensible approach is to limit its treatment to specialized cancer centers only.

In the literature, the question of the use of elective neck dissection (END) in carcinomas of the oral tongue and especially with regard to the extent of END (De Zinis et al., 2006; Huang et al., 2008; Khafif et al., 2001; Silver and Moisa, 1991) remains open. A decision is often made according to clinical nodal status (cN+/-) or T-stage (T1–4). As mentioned above, for carcinomas of the oral cavity in general, END is recommended at least for the ipsilateral levels I–III (according to Robbins et al., 2002) in all patient cases, irrespective of the pre-interventional cN status (Wolff et al., 2012). A bilateral END approach for tongue carcinomas is sometimes favored in more advanced primary tumors, e.g., T3–4 tumors that cross the tongue's midline or in patients with initially positive lymph node metastasis (Koo et al., 2006; Lim and Choi, 2007; Lim et al., 2006). The literature still lacks concise recommendations concerning this issue of the extent of END in unilateral tongue carcinomas. Depending on the opinions and routines of the department carrying out the treatment, the neck dissection protocol for these patients usually ranges from the removal of ipsilateral levels I–III to the removal of both bilateral levels I–III.

The purpose of this study has been to clarify the remaining questions concerning the optimal extent of END treatment in patients with unilateral OTSCC. Another aim of this study has been to retrospectively analyze patient data from two hospitals, in both of which oral and maxillofacial surgery is undertaken, in order to help to identify the ideal level of END extension.

2. Material and methods

2.1. Study design

To address the raised questions regarding the benefit and optimal extent of END in patients with unilateral OTSCC, a retrospective cohort study was designed.

2.2. Study sample

The study sample consists of two different cohorts of OTSCC patients, distinguished from each other in the form of END treatment received. To be included in the general study population, patients had to be diagnosed with T1–2 OTSCC. The primary tumor lesion had to be limited to only one side of the tongue (e.g., right or left side) and was not allowed to cross the midline of the tongue. In the first contributing department (Department of Oral and Maxillofacial Surgery of the Technische Universität Munich [TUM]), all included patients presented for treatment of unilateral OTSCC between December 2006 and July 2015, and in the second contributing department (Department of Oral and Maxillofacial Surgery of the Ludwig-Maximilians-Universität Munich [LMU]), the included patients were treated between February 2007 and April 2015.

In the first department (TUM), the preferred treatment strategy consisted of surgical removal of the primary tumor lesion and ipsilateral neck dissection, extending from levels I–III. In the other department (LMU), the preferred END treatment protocol, in contrast, favored bilateral removal of levels I–III. In the department performing ipsilateral END, intraoperative rapidly frozen sections were taken from all patients for pathological examination. If tumor-positive lymph nodes were found, neck dissection was immediately extended to the ipsilateral levels IV–V and to the contralateral levels I–III. Tumor aftercare usually featured continuous clinical controls every 3–6 months and a computed tomography scan each year.

2.3. Data collection methods

The data from the universities' interdisciplinary boards for head and neck tumors were screened retrospectively for patients with matching criteria. Additional relevant clinical data of indexed patients were then retrieved via the universities' clinical file management system at both institutions.

2.4. Variables

General patient data were screened for information such as age, gender, preoperative staging results, surgical reports, histopathological findings (e.g., TNM stage), interdisciplinary tumor board recommendations, and postoperative treatment procedures.

2.5. Data analysis and statistical calculations

The collection and analysis of the study's data was approved by the university's local ethics committee (registration numbers 2777/10 and 383/15). The research was conducted in accordance with the Declaration of Helsinki. The patient data from both participating institutes were combined, and statistical analysis was performed to obtain information on the rate of positive lymph nodes in the END and on later nodal metastasis during follow-up. Possible predictors of the rate of occult or future lymph node metastasis (e.g., gender, age) were sought. SPSS 22.0.0 software (IBM SPSS, Inc., Chicago, IL, USA) was used for statistical calculations. Descriptive and inferential statistics were computed by using the two-sample t test, chi-squared test, or Fisher exact test. Recurrence-free survival was assessed by using the Kaplan–Meier estimator. Differences between ipsilateral and bilateral neck dissections with regard to recurrence-free survival were examined by using Cox proportional hazard models. All analyses were conducted by using the survival package in R version 3.2.4 (R-Core-Team; Therneau and Gambsch). A p value of less than 0.05 was considered to be statistically significant.

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