Elective neck dissection vs observation in transorally treated early head and neck carcinomas with cN0 neck

GEORGIOS PSYCHOGIOS, M.D., PH.D., KONSTANTINOS MANTSOPOULOS M.D., PH.D., MICHAEL KOCH M.D., PH.D., NILS KLINTWORTH M.D., PH.D., MARCUS KAPSREITER M.D., PH.D., JOHANNES ZENK M.D., PH.D. & HEINRICH IRO M.D., PH.D.

Department of Otorhinolaryngology, Head and Neck Surgery, Friedrich Alexander University of Erlangen-Nuremberg, Erlangen, Germany

Abstract

Conclusion: This study showed that elective neck dissection (ND) resulted in reduced regional recurrences in a selected group of surgically treated patients with pT1-2 carcinomas but did not show any benefit for disease-specific survival (DSS). Furthermore, the importance of pN classification was also verified for this patient group. *Objectives:* The aim of this study was to determine whether the use of elective ND in patients with early head and neck carcinomas and cN0 neck that have undergone a transoral removal of the primary tumor can reduce the incidence of regional recurrence and improve survival. *Methods:* Between 1980 and 2010, 224 patients that underwent transoral resection of a pT1-2 carcinoma and had a cN0 neck were included in the study; 101 patients received an elective ND and 123 did not. *Results:* The group that underwent elective ND showed a tendency toward better regional control (RC) (96.0% vs 90.3%, $p = 0.07$) but similar DSS (85.7% vs 85.4%, $p = 0.984$). Cases with pN0 classification had a better overall survival (74.6% vs 46.9%, $p = 0.07$), DSS (88.4% vs 53.6%, $p = 0.44$), and RC (98.6% vs 62.5%, $p < 0.001$) compared with pN+ patients.

Keywords: *Cervical metastases, regional recurrence, occult metastases, elective treatment, N0 neck*

Introduction

Management of cN0 neck is a subject of ongoing debate in head and neck oncology [1]. The use of transoral laser resection in most early head and neck carcinomas further complicated the dilemma of optimal neck treatment [2,3]. In contrast to a transcervical approach where neck dissection (ND) is part of the operation, in cases where the primary tumor is removed transorally an ND adds significantly to the magnitude, duration, and perhaps to the morbidity of the treatment. Elective ND is generally accepted if the probability of occult metastasis is 15–20% or more [4]. In such cases the danger of regional recurrence outweighs the possible morbidity of elective ND. This percentage was mainly determined in a study by Weiss et al., who performed a mathematical analysis and concluded that the benefits outweigh the costs of elective ND only when the risk for occult metastasis exceeds 20% [5].

In previous studies we showed that all but glottic carcinomas of the head and neck region have an incidence of occult cervical metastases greater than 20% even in pT1-2 classification [6–10]. The aim of this study was to determine whether the use of elective ND in patients with early head and neck carcinomas and cN0 neck that have undergone a transoral removal of the primary tumor can reduce the incidence of regional recurrence and improve survival.

Correspondence: Georgios Psychogios, Department of Otorhinolaryngology, Head and Neck Surgery, Friedrich Alexander University of Erlangen-Nuremberg, Waldstrasse 1, 91054 Erlangen, Germany. Tel: +49 9131 8533156. Fax: +49 9131 8533833.
E-mail: Georgios.Psychogios@uk-erlangen.de, gpsychogios@gmail.com

Material and methods

A retrospective study was conducted at an academic tertiary care center. The main inclusion criterion was previously untreated head and neck squamous cell carcinoma (HNSCC) with definitive surgical treatment as a monotherapy between 1980 and 2010. The selected patients all had preoperative cN0 cervical status and had undergone a primary transoral removal of the primary tumor with or without elective ND as part of the primary surgical treatment. Those finally selected were all patients who proved to have a pT1-2-primary tumor. Because patients with early glottic carcinomas never received an elective ND in cases with cN0 status, the finally included patients had pT1-2 carcinoma of the oral, oropharyngeal, hypopharyngeal or supraglottic region. Patients previously treated for head and neck carcinomas or with histology other than squamous cell carcinoma (SCC) were excluded from the study. Also excluded were patients who received adjuvant radiotherapy or chemoradiation after the surgical treatment. Staging was re-evaluated after reviewing the surgical and pathology reports according to the 2010 American Joint Committee on Cancer (AJCC) and Union Internationale Contre le Cancer (UICC) classifications. Approval was obtained from the institutional review board of the hospital.

The end points for the analysis were regional control (RC) and disease-specific survival (DSS). Time to RC was calculated from the date of initial diagnosis to the date of the most recent clinical review when regional recurrence was confirmed. Regional recurrence was defined as metastatic carcinoma developing at the cervical lymph nodes after completion of initial treatment. DSS was defined using the time from the date of diagnosis to death from the cancer or complications of treatment. Calculations of 5-year overall survival (OS), DSS, and RC were made with Kaplan–Meier estimates and compared by means of log-rank test using 95% intervals. A p value of < 0.05 was considered significant. All statistical analyses were performed using SPSS version 19 (SPSS Inc., Chicago IL, USA) for Microsoft Windows.

Resection of the primary tumor was performed using transoral electrocautery in most cases where the tumor could be accessed directly, or transoral laser microsurgery (TLM) in cases where the tumor site was deeper (e.g. supraglottic, hypopharyngeal region). Surgery of the neck was performed simultaneously with the primary site procedure or shortly thereafter, once the definitive histology results from the primary tumor were available. A modified radical ND level Ib–V or a selective ND level II–IV was performed in most cases. In cases with involvement of the anterior oral region, level Ia was included. Typical indications for a bilateral elective ND were carcinomas near the midline such as anterior floor of the mouth, tongue and uvula, supraglottic carcinomas, and carcinomas of the posterior pharyngeal wall. In cases where unilateral ND was performed, the contralateral neck was assumed to be free from tumor metastases.

Standard preoperative diagnostics included clinical examination, ultrasonography, and computed tomography (CT). Magnetic resonance imaging (MRI) was performed in only a few cases. The use of ultrasound in the diagnostic approach to lymph node metastases has a long tradition in our department and is performed by the otorhinolaryngologist. We have been using high-end sonography devices since 1990 and acquired an Acouson 2000 (Siemens, AG) in 2007. The decision as to neck treatment was made in our tumor board.

Results

A total of 1305 transorally treated patients with pT1-2 carcinomas of the head and neck region were identified; 766 glottic carcinomas, 277 cases with adjuvant radiotherapy, and 38 cases with adjuvant radiochemotherapy were excluded. The final study population included 224 patients who met the inclusion criteria. The median age at presentation was 59 years, ranging from 37 to 85 years (SD 11.2). In all, 177 (79.0%) of the patients were men and 47 (21.0%) were women, with a male to female ratio of 3.8:1. Detailed patient characteristics are presented in Table I. The OS of the whole group was 69.7%, DSS was 85.5%, and RC 92.7%.

Of the 224 patients, 101 received an elective ND and 123 followed a wait and see policy. Fifty-six patients underwent a unilateral ND and 45 a bilateral ND. Of the unilaterally treated patients, 34 underwent a modified radical ND and 22 a selective ND. Of the bilaterally treated patients, 33 underwent a modified radical ND and 12 a selective ND. Table II shows the pN classification of the patients. A median number of 21 (range 9–56) lymph nodes was identified in each cervical side after neck dissection. The ND upgraded the clinical N classification in 10 of 101 operated patients, resulting in an occult metastasis rate of 9.9%. The 21 metastatic lymph nodes had a maximal diameter of 6–24 mm with a mean of 17 mm. None of the lymph node metastases showed perinodal invasion.

Of the 101 patients post ND only 3 suffered a regional recurrence, resulting in an RC estimate of 96.0%. On the other hand, 10 of 123 patients without ND had regional metastases in the follow-up period,

Table I. Characteristics of patients.

Characteristics	Total number of patients (relative frequency in %)
Age (years)	
Mean	59.1
Median	59.0
Range	37–85
Follow-up (months)	
Mean	61.8
Range	3–216
Gender	
Male	177 (79.0%)
Female	47 (21.0%)
Smoking habits	
Smoker	170 (75.9%)
Ex-smoker	12 (5.4%)
Non-smoker	42 (18.7%)
Surgical technique	
TLM	94 (42.0%)
Electrocautery	130 (58.0%)
Differentiation	
Well differentiated	49 (21.9%)
Moderately differentiated	119 (53.1%)
Poorly differentiated	48 (21.4%)
Not differentiated	8 (3.6%)

TLM, transoral laser microsurgery.

resulting in an RC of 90.3% (Figure 1). Statistical analysis revealed a tendency toward a better RC in the ND group ($p = 0.076$), but the small number of events weakened statistical power. On the contrary, OS (72.4% vs 67.4%, $p = 0.197$) and DSS (85.7% vs 85.4%, $p = 0.984$) were similar in both groups.

pN classification proved to have significant prognostic relevance for the patients. Cases with pN0 classification had a better OS (74.6% vs 46.9%, $p = 0.007$), DSS (88.4% vs 53.6%, $p = 0.44$), and RC (98.6% vs 62.5%, $p < 0.001$) compared with pN+ patients. The power of statistical analysis was weakened by the difference in the number of patients in each group.

Table II. N classification according to pT classification.

	No ND	pN0	pN1	pN2b	pN2c	All
pT1	87	55	0	3	1	146
pT2	36	36	3	2	1	78
All	123	91	3	5	2	224

ND, neck dissection.

In all, 146 patients had a pT1 tumor and 78 had a pT2 tumor. The median tumor size was 15 mm (range 5–39 mm) and the median tumor depth was 4 mm (range 1–23 mm). Tumor depth was measured using an imaginary line reconstructing the basal membrane of the healthy mucosa to the deepest point of tumor invasion. No correlation between tumor depth and regional disease could be found. In 72 (32.1%) patients the primary tumor was in the oral cavity, in 63 (28.2%) in the oropharynx, in 17 (7.6%) in the hypopharynx, and in 72 (32.1%) in the supraglottic region. The incidence of regional recurrences was not sufficiently high to permit statistical analysis of the results for each anatomic region separately.

Discussion

It is well known that the presence of cervical lymph node metastases is the most important prognostic factor for head and neck carcinomas. Thus treatment of the neck plays a central role in the management of these carcinomas [11]. Nevertheless the best treatment modality in case of clinical absence of cervical metastases is still discussed very controversially [1,12–15]. It is characteristic that the same group of nominated authors published two review articles in recent years; the first review concluded that an elective ND should be performed in surgically treated patients if the risk of occult metastases was more than 20% [4]. On the other hand, the second review concluded that elective ND does not seem to be superior to a wait and see policy [2].

It is true that elective ND represents a compromise. Surgeons accept overtreatment of a number of patients in order to provide optimal treatment to the rest. On the other hand, a wait and see policy carries the risk that occult metastases, which can easily be cured, could progress in a potentially incurable disease. So where does the ideal cut-off point of occult cervical metastases rate lie for choosing between elective ND and watchful waiting? Much of the problem of finding the ideal treatment modality seems to be the fact that this cut-off point is definitively not a fixed number. It is a risk–benefit calculation of many factors that can change over time and can also be different in various regions and for individual patients. Weiss et al. proposed a cut-off point at 20% and suggested performing elective ND if the likelihood of occult metastasis was estimated to be more than 20% [5]. However, an improvement of elective ND in terms of effectiveness, morbidity, hospital stay, and costs would lower the ideal cut-off point (Figure 2) [16]. On the other hand, a similar improvement of salvage ND would increase the same threshold [17]. An important role is also played by the accuracy of

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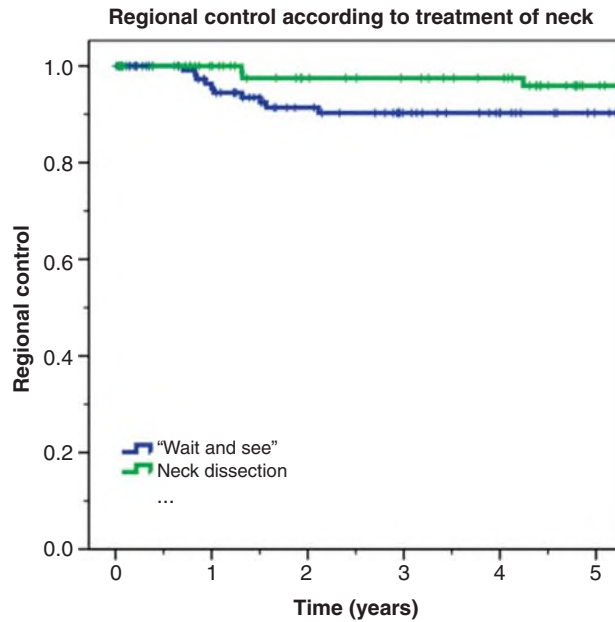**Regional control according to treatment of neck**

Figure 1. Regional control according to treatment of the neck.

follow-up and the compliance of the patient, because they can lead to early detection of delayed cervical metastases and indirectly improve the effectiveness of salvage ND (Figure 2).

The present study included a highly selected patient collective with an occult metastases rate of about 10%, which is less than half of the incidence found in a previous study by our department in a similar patient group [9,18]. The reason is that in most cases where cervical lymph node metastases were identified in the ND an adjuvant therapy had been additionally applied. However, inclusion of a large number in a homogeneous patient group treated without adjuvant therapy is the big advantage of this study because it facilitates examination of the impact of elective ND alone in a defined patient group.

The main finding of the present study is the improved RC of the group with elective ND. In fact there were three times more regional recurrences in the group treated with the wait and see policy. Nevertheless, delayed lymph node metastases were
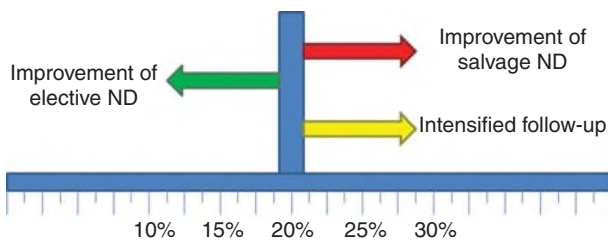

Figure 2. Influence of various parameters in the ideal cut-off point of occult cervical metastases rate for choosing between elective neck dissection (ND) and watchful waiting.

also found after elective ND. This is consistent with the literature and emphasizes the need to dissect all necessary cervical levels during operation [19]. It also points out the importance of frequent follow-up of the patients. On the other hand DSS and OS did not differ significantly in the two groups, perhaps reflecting the low incidence of occult metastases in this highly selected study group. Other studies also found it difficult to show an improvement of survival after elective ND [2].

ND has the advantage of being not only a therapeutic procedure but also a diagnostic and staging procedure. The other important finding of this study is the prognostic significance of pN classification. Patients with pN+ neck had worse OS, DSS, and RC, which indicates that they should have been treated with adjuvant radio(chemo)therapy. This fact highlights the diagnostic value of elective ND, which makes it possible to avoid adjuvant therapy in cases with pN0 neck. Thus additional morbidity can be avoided and radiotherapy can be reserved for regional relapse or second malignancies.

The extent of ND is another important issue. In the present study, most of the patients underwent a modified radical ND, although in recent years we have usually performed selective ND in cases with clinically N0 neck. There are many studies in the literature that propagate the use of selective ND because it has a reduced morbidity with comparable oncologic effectiveness [2,11,16,20]. To further minimize morbidity, the concept of sentinel lymph node biopsy (SLNB) has been tried with partial success, mostly in oral/oropharyngeal carcinomas in

recent years. Nevertheless, SLNB in HNSCC is currently only employed in clinical trial settings and has not yet found acceptance in everyday clinical practice.

Conclusion

This study showed that elective ND resulted in reduced regional recurrences in a selected group of surgically treated patients with pT1-2 carcinomas but did not show any benefit for DSS. Furthermore the importance of pN classification was also verified for this patient group.

Acknowledgment

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