

Surgical treatment of locally limited tonsillar cancer

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Introduction

In the United States, approximately 5000 new cases of oropharyngeal cancer are diagnosed annually, of which 85–90% are squamous cell carcinomas (SCC) [1]. Although SCC of the oropharynx is diagnosed predominantly in people over the age of 45 years, western European and American studies suggest that the incidence of the disease in the under-45s has increased over the past 20–30 years [2]. There is rapidly emerging literature on the role of HPV in the oncogenesis of oropharyngeal SCC [3].

It is said that 70–80% of oropharyngeal SCCs originate in the tonsillar complex [4]. Management of tonsillar complex tumors is based on the clinical or pathological stage, comorbidities and patient preferences, whereas institutional biases seem to have an important role [4]. Single modality therapy (surgery or primary radiotherapy) has been proposed in the early stages, reserving combinations of these, possibly with chemotherapy, for advanced stages [3,4]. The purpose of the present study was to evaluate the experience of a single head and neck oncology referral center in the primary surgical management of T1-2 tonsillar squamous cell carcinoma. Furthermore, we aimed to provide information on decision making in the management of the neck and examine whether surgical neck staging would allow more rational use of adjuvant therapy in early local tonsillar carcinomas.

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Materials and methods

A retrospective study was conducted at an academic tertiary referral center (Department of Otorhinolaryngology, Head and Neck Surgery, University of Erlangen-Nuremberg, Erlangen, Germany). The records of all patients treated with primary surgery for T1 and T2 tonsillar carcinomas between 1977 and 2005 were evaluated. Patients previously treated for this cancer, second primary tumors, systemic disease at the time of diagnosis, or histology other than squamous cell carcinoma were excluded from the study.

Staging was conducted according to the 2002 American Joint Committee on Cancer (AJCC) and Union Internationale Contre le Cancer (UICC) classification [5]. All patients were evaluated preoperatively by physical examination, sonography of the neck and, in many cases, contrast-enhanced computed tomography.

All study cases were evaluated for 5-year overall survival (OS), 5-year disease-specific survival (DSS) and local control (LC) rates, with respect to T stage, N classification, surgical margins (R status), and adjuvant therapy. Furthermore, we looked at the regional metastatic behavior of early local tonsillar carcinomas, with respect to decisions on neck management. Cases were also evaluated for incidence of major complications and incidence of related (temporary or permanent) tracheotomies. Major complications were defined as those which necessitated prolonged hospitalization, blood transfusion, additional surgery or admission to the intensive care unit. Adjuvant treatment had been determined by an interdisciplinary tumor board and consisted of postoperative radiotherapy to the primary tumor site and both sides of the neck, either alone or combined with chemotherapy. Adjuvant therapy was indicated in cases with presence of positive surgical margins when further surgery was not feasible, advanced neck disease, tumor infiltration depth of more than 5 mm, extracapsular tumor spread and infiltration of lymph vessels or nerves on permanent histology.

Overall survival estimate (OS) was defined as the percentage of patients who were still alive within 5 years divided by the total number of patients. Five-year disease-specific survival rate estimate (DSS) was defined using the time from the date of diagnosis to death from the cancer or complications of treatment. Time to Local control (LC) was calculated from the date of initial diagnosis to the date of the most recent clinical review when local recurrence was confirmed. Local recurrence was defined as invasive carcinoma developing at the anatomic site of the primary tumor after completion of initial treatment. Statistical analysis was performed using the Kaplan–Meier method with 95% confidence intervals. The software SPSS v19 for Windows (SPSS Inc., Chicago, IL) was used for the analysis. A *p* value of <0.05 was considered statistically significant.

Results

A total of 209 cases were included in this study. There were 155 men and 54 women, giving a ratio of 2.9:1. Mean age was 55.43 years (range –83, SD 10.68). Mean follow-up period was 77 months. Transoral resection of the tumor was performed in 198 cases (laser 32, conventional 42, with electric knife 124) and via the transcervical approach in 11 cases. A transcervical approach was indicated in cases of deep infiltration of the lateral pharyngeal wall and proximity of the tumor to adjacent vital structures. Overall survival was 63.5%, DSS was 81.6%, while LC was 91.6% in this series.

Table 1 gives details of the survival data according to the parameters of our analysis. T1 cases showed a tendency to better survival compared with T2 tonsillar tumors. Moreover, OS and DSS were significantly better for R0 cases in comparison with R+ cases.

Additionally, OS was significantly worse for patients with advanced neck disease, pN2-3 (Table 1). As to the impact of contralateral metastasis on survival, our analysis did not detect a significant difference between cases with and without contralateral metastases in terms of disease-specific (*p* = 0.51) and overall survival (*p* = 0.64). This finding should be viewed with reservations because of the very small number of cases with contralateral metastasis (9).

Of the 209 patients in the study sample, 198 underwent neck dissection (198/209, 94.7%). Sixty-four had pN0 status, 26 patients were pN1, 96 patients pN2 and 12 patients pN3. Neck dissection was performed in 38 of the 47 patients with cN0 status, and seven of them were found to be pN+ (four pN1, two pN2b and one pN2c). The occult metastasis rate was therefore 18.4%. Four of these seven patients had T1 and three had T2 primary tumors.

Bilateral neck dissection was carried out in 77 cases, and metastases were found on the contralateral side (pN2c stage) in nine cases (11.7%): one was cN0, one was cN2b, and seven were cN2c. Clinically negative but pathologically positive contralateral lymph nodes were detected in 2/45 cases (4.4%). Of the 33 cases with an ipsilateral clinically positive neck that underwent bilateral neck dissection, contralateral occult lymph node metastases were found in only one case (3%). Surgical staging altered clinical staging in 67/198 cases (33.8%) (Table 2). In our patient collective (consisting of T1–T2 cases only), no high incidence of metastasis and no regional recurrence in the retropharyngeal lymph nodes was observed.

Major complications in this series were detected in 14.3% of our cases (Table 3). None of these complications was fatal. Temporary tracheotomies were necessary in 23 cases (11%), whereas permanent tracheotomies were needed in only nine cases (4.3%).

Discussion

Carcinomas arising from the tonsillar region present a clinical dilemma, due to the lack of prospective randomized trials and site-specific analyses [3]. Treatment decisions have therefore to be based mainly on retrospective data [6]. Despite the flaws of retrospective studies, the data obtained could be useful in decision making and could improve treatment planning. To the best of our knowledge, the case series of surgically managed locally limited tonsillar carcinoma presented here is the largest in the literature.

The surgical treatment of tonsillar carcinomas evolved, parallel to experience, over the years. At the beginning, surgical treatment was more radical with tracheotomies performed in more cases and more frequent bilateral neck dissections in cN+ cases. Laser was introduced in 1979 for surgical treatment of tonsillar tumors in our clinic. Moreover, until 1999, reconstruction of the pharyngeal defect by transcervical cases was performed using a pectoralis major myocutaneous flap. Since then, a reconstruction with a radial forearm flap has been preferred. Fasciocutaneous flaps were indicated when thinner, less bulky flaps were required. On the other

Table 1

Overall survival (OS), disease-specific survival (DSS) and local control (LC) rates for the study variables investigated.

Parameter (number of patients)	OS (%)	DSS (%)	LC (%)
T1 (87) vs. T2 (122)	70.2 vs. 58.8, <i>p</i> = 0.061	87.5 vs. 77.2, <i>p</i> = 0.175	94.5 vs. 89.6, <i>p</i> = 0.33
OP (43) vs. OP + R(C)T (166)	69.9 vs. 61.1, <i>p</i> = 0.664	84.2 vs. 81.1, <i>p</i> = 0.805	88.4 vs. 92.4, <i>p</i> = 0.253
R0 (179) vs. R+ (30)	65.9 vs. 49.5, <i>p</i> = 0.02	84.9 vs. 62.2, <i>p</i> = 0.011	
N0-1 (90) vs. N2-3 (108)	72.2 vs. 55.3, <i>p</i> = 0.048	88.0 vs. 73.9, <i>p</i> = 0.098	

Table 2
Clinical and surgical N classification of the study cases.

Clinical N classification	Surgical N classification					
	pN0	pN1	pN2a	pN2b	pN2c	pN3
cN0	31	4	0	2	1	0
cN1	9	8	2	5	0	2
cN2a	1	2	7	8	0	2
cN2b	8	5	4	33	1	1
cN2c	15	7	5	19	7	4
cN3	0	0	0	2	0	3

hand, a radial forearm flap could not be used in cases of inadequate collateral blood flow to the hand via the ulnar artery, prior surgical or traumatic injury to the radial artery or poor vascular quality (e.g. arteriosclerosis).

The high disease-specific survival (81.6%) and local control (91.6%) rates found in our analysis, together with the relatively low complication rate, confirm that surgery can provide an effective and safe cure for locally limited tonsillar cancer. Satisfactory oncologic results were achieved even in cases with regional metastases.

In agreement with the relevant literature [7,8], positive surgical margins were found to be significantly associated with a worse prognosis, despite the fact that the majority of these patients (86.7%) were given some form of adjuvant therapy. Our analysis confirmed that surgeons should always aim for clear surgical margins, even if more than one resection is required. In terms of survival, adjuvant therapy did not seem to compensate for the residual tumor at the end of the surgical treatment.

On the contrary, in terms of the oncologic parameters of our study, no statistically significant difference was found between patients with and without adjuvant radio(chemo)therapy. This could possibly be due to the fact that the cases with combined therapy usually had worse prognostic factors, such as advanced neck disease, tumor infiltration depth of more than 5 mm, extracapsular tumor spread, and infiltration of lymph vessels or nerves seen on histology. It should not be forgotten, however, that adjuvant therapy protocols, indications and techniques have evolved considerably over recent years [9]. The lack of homogeneous criteria over time complicates the evaluation of this finding and could be regarded as a limitation of our study, which included patients treated during a period of almost 30 years.

Neck dissection was performed in 198 of the 209 patients in the study sample (94.7%). Eleven patients (5.3%) did not receive surgical neck treatment due to either refusal of therapy or comorbid medical problems. According to the literature, nodal metastasis is thought to be one of the most influential prognostic factors in tonsillar carcinomas. This was confirmed by our analysis: advanced neck disease (pN2-3) was detected in 54% of our cases and showed a trend toward a worse prognosis, even affecting overall survival to a significant extent. This emphasizes the crucial need for management of the cervical lymph nodes, even with locally limited tonsillar carcinomas.

Management of the neck by cN0 status, even for tumors in other head and neck regions, remains controversial [10,11]. Few would

argue that institutional bias has a major role in the treatment of neck disease [6]. The fact that the treatment of neck disease in head and neck cancer has changed with time could furthermore account for selection bias and may be viewed as a limitation of our study. According to the literature, 15–30% of all oropharynx cancer patients with cN0 neck status will eventually present with regional nodal metastases [3]. Similarly, our analysis of local early tonsillar carcinomas detected a not inconsiderable occult metastasis rate of almost 19%. Identification of occult cervical metastasis is an important determinant for staging and prognosis of these cases [12]. Consequently, neck management in the form of ipsilateral selective neck dissection or radiation should always be included in the therapeutic plan of N0 cases.

For anatomical reasons, the ipsilateral side is the more frequently invaded in cases of positive neck disease; contralateral metastasis remains unlikely [11]. Chung et al. analyzed 76 cases with tonsillar carcinomas (stages III-IV: 81.6 %) and found an overall contralateral metastasis rate of 40.9% [13], detecting significantly higher rates of contralateral metastasis by advanced local disease [13]. Chang et al. analyzed 43 cases with T1–T4 tonsillar carcinomas and found an overall contralateral metastasis rate of 16% [11]. Analyzing only T1–T2 cases, we detected a lower but still not inconsiderable rate (9/77, 11.7%). Interestingly, the majority of these cases (77.7%) already had clinically positive contralateral lymph nodes. In cases with a clinically positive ipsilateral side, we did not find a high incidence of contralateral metastasis (3%). Even with advanced ipsilateral neck disease, this rate remained remarkably low (4.2%). Consequently, management of the contralateral neck side in locally limited tonsillar tumors could possibly be reserved for clinical N2c status. Patient compliance should always be taken into consideration and regular follow-up is essential.

Neck dissection is thought to be a useful instrument in terms of staging and treatment planning. It identifies patients with occult disease, to whom adjuvant treatment should be given, and reduces radio(chemo)therapy-related morbidity by confirming the diagnosis of pN0 status [4]. In this way, adjuvant therapy is appropriately targeted and rationally applied [14]. Moreover, pathological staging could contribute to a more accurate assessment of the prognosis and to improvement of patient counseling. Interestingly enough, neck dissection altered clinical staging in more than one-third of our study cases.

As mentioned above, tracheotomy was on the whole performed more frequently in the early years of our analysis. Due to a learning curve in terms of surgical treatment and the necessity of tracheotomy, the number of tracheotomies decreased in the following years. Interestingly, 7/9 cases with permanent tracheotomies (77.7%) had received adjuvant therapy. A possible reason for a permanent tracheostoma in these cases could be a persistent swallowing dysfunction due to the adjuvant radiation. As known, apoptosis from chemoradiation could induce abnormal motility of the upper aerodigestive tract, resulting in stasis of the bolus and aspiration [15]. Moreover, long-term scarring may result in stenosis of the upper digestive tract [16].

A critical point of our study lies in the fact that the prognostic value of HPV infection in tonsillar carcinomas was not examined. There seems to be increasing data suggesting that survival of patients with HPV-positive oropharyngeal carcinomas is better with either primary chemoradiation therapy or surgery followed by adjuvant radiation [17–19], indicating that HPV-positive disease is more radiosensitive than HPV-negative disease [18,19]. Future studies should focus on implementing this knowledge in the treatment of such lesions and augmenting conventional forms of treatment by the addition of therapeutic vaccines and immunotherapy.

Table 3
Specific types and incidence of surgical complications.

Complication	Number of cases (%)
Bleeding	9 (30)
Aspiration	1 (3.3)
Fistula	5 (16.7)
Wound healing disorders	4 (13.3)
Nerve lesions	1 (3.3)
Other complications	10 (33.3)

Conclusion

In conclusion, primary surgical treatment of local early (T1-2) tonsillar carcinomas proved to be an effective and safe treatment modality with satisfactory oncologic results and a low rate of complications. Surgeons should always aim for clear surgical margins, especially as adjuvant therapy did not seem to compensate for an R+ situation at the end of surgical treatment. Moreover, our analysis showed that an aggressive approach to neck management is justified even in cN0 cases.

Conflict of interest statement

Authors have no conflicts of interest and no financial disclosures exist.

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