

Relevance of Oropharyngeal Cancer Lymph Node Metastases in the Submandibular Triangle and the Posterior Triangle Apex

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Abstract. *Background:* Neck dissection of levels I and IIB is time consuming and can cause several comorbidities. The aim was to analyze whether levels I and IIB need to be dissected in patients with oropharyngeal cancer and clinical N0 or N+ neck. *Patients and Methods:* A retrospective analysis of 77 patients with oropharyngeal cancer was carried out with evaluation of the incidence of neck node metastasis in levels I and IIB. *Results:* None of the patients with cN0 neck had metastases in level I or IIB; 12.8% of the patients with cN+ neck had metastases in level I, 35.1% in level IIA and 25.6% had metastases in level IIB. *Conclusion:* Levels I and IIB should be dissected in cN+ neck in order to achieve maximal oncological safety. The preservation of levels I and IIB in cN0 neck seems to be justified in terms of improving functional results and concomitant reduction of operation time.

The presence of cervical lymph node metastases is one of the most important prognostic factors for patients with head and neck cancer. In this patient group, lymph node metastasis is associated with a decrease in survival of up to 50% depending on the localization and extent (1, 2). Current clinical staging modalities (palpation supplemented by current imaging methods and ultrasound-guided fine-needle aspiration cytology) are unable to reliably predict subclinical metastases. Current publications report on a sensitivity rate of about 70-80% for the detection of cervical metastases by sonography, magnet resonance imaging (MRI), computed tomography (CT) and ¹⁸F-fluorodesoxyglucose (FDG)-positron-emission

tomography (PET) as well as PET/CT (3-7). The incidence of clinically occult metastasis for patients with carcinomas of the oropharynx still amounts to 20% (8-10).

The insufficient sensitivity of non-invasive examination methods as well as the high risk of locoregional recurrences and distant metastases in cases of wait-and-see strategy are justification for elective treatment of the clinical N0 neck (11) which can be performed by surgery or radiotherapy. A significant advantage of elective neck dissection in comparison to radiotherapy is its value as a staging procedure. The histopathological examination of the neck dissection specimen delivers exact information on the metastatic spread and offers the ability to optimally plan adjuvant therapy.

The surgical therapy of patients with head and neck carcinomas and clinical N+ neck is less controversially discussed than the treatment of the clinical N0 neck. Currently, many head and neck departments worldwide still perform standard radical neck dissection (RND) or modified radical neck dissection (MRND) in cases of clinical N+ neck (12). In some institutions, selective neck dissection (SND) is also a treatment alternative for those patients in selected cases (12-14). Some evaluations show that the performance of SND, especially combined with postoperative radiotherapy, is a possible therapeutic option (12, 15, 16). Prospective multi-institutional studies comparing the therapeutic effect of SND and MRND are still lacking so that the significance of SND for patients with clinical N+ neck is currently under debate.

As therapy of choice for elective treatment of patients with carcinomas of the oropharynx, many authors recommend SND (II-IV) (17-20). Some authors also recommend SND (I-III) or SND (I-IV) as reasonable treatment strategy for patients with oropharyngeal cancer (21-24). The operative dissection of levels I and IIB requires time-consuming preparations because of their anatomic location and is associated with a higher morbidity, often leading to postoperative sequelae with a negative impact on quality of life. Damage of the mandibular branch of the facial nerve and the hypoglossal nerve has been reported, especially after dissection of level I. Furthermore, the

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Table I. Type of neck dissection performed.

Type of neck dissection	Cases
RND ipsilateral	1.3% (n=1)
MRND ipsilateral	53.2% (n=41)
SND (I-III) ipsilateral	2.6% (n=2)
SND (II-IV) ipsilateral	2.6% (n=2)
SND (II-V) ipsilateral	1.3% (n=1)
RND ipsilateral, MRND contralateral	2.6% (n=2)
RND ipsilateral, SND (I-III) contralateral	1.3% (n=1)
RND ipsilateral, SND (II-IV) contralateral	1.3% (n=1)
MRND bilateral	6.5% (n=5)
MRND ipsilateral, SND (I-III) contralateral	5.2% (n=4)
MRND ipsilateral, SND (I-IV) contralateral	7.8% (n=6)
MRND ipsilateral, SND (II-III) contralateral	1.3% (n=1)
MRND ipsilateral, SND (II-IV) contralateral	3.9% (n=3)
SND (I-III) bilateral	3.9% (n=3)
SND (II-IV) bilateral	3.9% (n=3)
SND (I-IV) ipsilateral, SND (I-III) contralateral	1.3% (n=1)

RND, Radical neck dissection; MRND, modified RND; SND, selective neck dissection.

dissection of level I is complicated by the complex anatomy of the structures surrounding the submandibular gland such as the lingual and facial artery, the lingual nerve, the facial vein and the mandibular branch of the facial nerve, which make the dissection technically demanding.

Dissection of level IIB requires traction of the accessory nerve in many cases to achieve an optimal access to the lymph nodes. Shoulder dysfunction due to damage to the accessory nerve is the most common morbidity associated with neck dissection. Dissection of level IIB can also be complicated by frequent bleeding from a branch of the occipital artery. These complications may be avoided through the preservation of level I and IIB lymph nodes during neck dissection, so that the question is whether the omission of level I and IIB dissection leads to an impairment of the oncological result. Therefore, the aim of the present study was to identify the incidence of level I and IIB metastasis in patients with oropharyngeal carcinomas who received surgical treatment as initial therapy and furthermore to clarify whether the dissection of level I and IIB is necessary for treatment of N0 and N+ neck in patients with squamous cell carcinoma of the oropharynx.

Patients and Methods

Patients with squamous cell carcinoma of the oropharynx who underwent surgical treatment for the primary lesion and therapeutic or elective neck dissection from April 1998 to August 2008 were included. Patients who underwent primary radiochemotherapy were excluded. Based on these criteria, 77 patients were identified.

The following data were obtained from patient charts: sex, primary lesion site, TNM status, operative procedure (especially

Table II. TN classification of the patient population (all patients classified M0).

	N0	N1	N2a	N2b	N2c	N3	Total
T1	15	3	1	7	0	0	26
T2	18	3	2	13	3	1	40
T3	2	1	0	3	0	1	7
T4	1	1	0	0	2	0	4
Total	36	8	3	23	5	2	77

type of neck dissection), number and level of cervical lymph node metastases. The clinical neck status was determined on the basis of the initial ultrasound examinations. Lymph nodes with a size of more than 10 mm were considered as suspicious for metastases.

After extirpation, the neck dissection specimens were stored separately according to the neck level and then sent for histological examination to the Institute of Pathology. Histological examination of metastases included the number and location of the nodes containing metastatic disease in levels I, IIA and IIB. The pathological T and N stage according to the UICC (25) were determined by evaluation of the pathological reports, while the M stage was classified from radiological findings.

The data were archived in an SPSS-based database (SPSS, version 10.0.7, SPSS GmbH Software, Munich, Germany) and statistically evaluated. The calculation of the 95% confidence interval (CI) was performed according to the method of Clopper and Pearson (26). Fisher's exact test was used to analyze if patients with cN+ neck have a significantly higher risk of metastasis. P-values <0.05 were considered to be statistically significant.

Results

Altogether, 77 patients with squamous cell carcinomas of the oropharynx fulfilled the inclusion criteria. In 3 cases, the tumor extended to the hypopharynx. Crossing of the midline was observed in 6 patients. Another 5 patients had bilateral tumor growth. The majority of patients, 76.6% (n=59), were male. The average age of the patients was 56.5 years (range: 40-80.7 years).

Overall, 107 neck dissections were performed. The ipsilateral lymph nodes were treated in all 77 patients. The contralateral neck side was additionally treated in 30/77 patients. In 38/77 cases, the ipsilateral neck was clinically staged N0 and in 39 cases N+. Contralateral neck dissection was performed in 28 patients with N0 neck, while in 2 cases contralateral neck dissection was performed in a clinical N+ situation. The types of neck dissection performed in this patient population are summarized in Table I.

In none of the patients did primary staging reveal the presence of distant metastases, so that all tumors were classified as M0. The distribution of stages according to the UICC is given in Table II.

Table III. Distribution of lymph node metastases at level I, IIA and IIB.

	Total			cN0			cN+		
	ND, n	pN+, n	Percentage (95% CI) ^a	ND, n	pN+, n	Percentage (95% CI) ^b	ND, n	pN+, n	Percentage (95% CI) ^c
Ipsilateral total	77	41	53.2 (41.5-64.7)	38	2	5.3 (2.9-13.9)	39	39	100 (90.1-100)
Level I	71	5	6.5 (2.1-14.5)	33	0	0 (0-9.2)	38	5	12.8 (4.3-27.4)
Level II total	77	32	41.6 (30.4-53.4)	38	2	5.3 (2.9-13.9)	39	30	76.9 (60.7-88.9)
Level IIA	77	27	35.0 (24.5-46.8)	38	2	5.3 (2.9-13.9)	39	25	64.1 (47.2-78.8)
Level IIB	77	10	13.0 (6.4-22.6)	38	0	0 (0-9.2)	39	10	25.6 (13.0-42.1)
Only other levels		7			0			7	
Contralateral total	30	5	6.5 (2.1-14.5)	28	3	4.0 (0.8-11.2)	2	2	100 (15.8-100)
Level I	20	0	0 (0-4.7)	18	0	0 (0-4.5)	2	0	0 (0-84.2)
Level II total	30	4	5.2 (1.4-12.8)	28	2	2.7 (0.3-9.3)	2	2	100 (15.8-100)
Level IIA	30	4	5.2 (1.4-12.8)	28	2	2.7 (0.3-9.3)	2	2	100 (15.8-100)
Level IIB	30	0	0 (0-4.7)	28	0	0 (0-4.5)	2	0	0 (0-84.2)
Only other levels		1			1			0	

ND, Neck dissection; pN+, pathologically confirmed metastases; cN0, clinical N0 neck; cN+, clinical N+ neck; CI, confidence interval. ^aPercentages relate to 77 patients; ^bipsilateral: percentages relate to 38 patients with cN0 neck; contralateral: percentages relate to 75 patients with cN0 neck (28 patients + 47 patients who were not operated contralaterally); ^cipsilateral: percentages relate to 39 patients with cN+ neck; contralateral: percentages relate to 3 patients with cN+ neck.

Level I was dissected in 71/77 patients. In 51 patients, only the ipsilateral level I was treated while in 20 cases, level I was dissected bilaterally. In 5 patients, metastases were detected histologically. These 5 patients also had clinical N+ neck. In all cases, the ipsilateral neck side was affected. Fisher's exact test revealed a significantly higher risk of metastasis in level I in case of a cN+ neck ($p < 0.05$). In 3 cases, metastases were detected synchronously in level IIA of the same side. Among the 5 patients with metastases in level I, there was 1 patient with a tumor reaching the hypopharynx. In 1 case, bilateral tumor extent was found. In 3 cases, the primary tumors were classified as pT2N2b and in one case each pT2N2c and pT4N2c, respectively.

The lymph nodes in level II were dissected ipsilaterally in all 77 patients. In 30 cases, additionally contralateral level II was dissected. Metastases were found in this region in 32 patients; these were located in 22 cases exclusively in sublevel IIA, in 5 cases exclusively in sublevel IIB, and in 5 cases in both subregions. In 27 patients, metastases were detected histologically in the area of level IIA, in 23/27 cases the metastases were located only on the ipsilateral side. Bilateral metastatic spread was found in 4 cases. Ipsilateral metastases were detected in 2 cases of clinical N0 neck as well as in 25 cases of clinical N+ neck. Contralateral metastases occurred in 2 patients with clinical N0 neck where the ipsilateral neck side was classified N+. The other 2 patients with contralateral metastases in level IIA had clinical N+ necks. In 3 cases, ipsilateral metastases were located in level IIA with metastases in level I, as well as in 5 cases associated with metastases in level IIB. The primary

tumor was limited to the oropharynx in 26 patients, while in one case the hypopharynx was also infiltrated. In 3 cases, crossing of the midline was detected. In 2 patients, bilateral tumor extent was revealed.

Lymph node metastases were detected in 10 patients in ipsilateral level IIB. There were no metastases on the contralateral side. All 10 patients had preoperative clinical N+ neck. Fisher's exact test revealed a significantly higher risk of metastasis in level IIB in case of a cN+ neck ($p < 0.05$). In 5 out of 10 cases, synchronous metastases were found in the ipsilateral level IIA. In 1 case, an isolated metastasis was detected in level IIB. In one out of the 10 patients, the tumor had crossed the midline. In another patient, bilateral tumor extent was found. The tumor was classified pT2N2b in 4 cases. In 2 cases, the tumor size was classified T3 with a cervical lymph node status corresponding to N2b situation. In one case each, the classification was pT1N1, pT2N2a, pT2N2c, and pT3N3, respectively. The distribution of the cervical lymph node metastases at levels I, IIA, and IIB is described in Tables III and IV.

Discussion

The dissection of levels I and IIB during neck dissection requires time-consuming preparation because of their anatomic location. This leads to an increased operation time. The inclusion of level I is moreover associated with a higher risk of bleeding (27). Removal of level IIB lymph nodes bears the risk of injuring the accessory nerve by traction, which is sometimes inevitable, or by interruption of its

Table IV. Distribution of lymph node metastases at level I, IIA and IIB related to the patients who underwent dissection of the respective level.

	Total			cN0			cN+		
	ND, n	pN+, n	Percentage (95% CI) ^a	ND, n	pN+, n	Percentage (95% CI) ^a	ND, n	pN+, n	Percentage (95% CI) ^a
Ipsilateral total	77	41	53.2 (41.5-64.7)	38	2	5.3 (2.9-13.9)	39	39	100 (90.1-100)
Level I	71	5	7.0 (2.3-15.7)	33	0	0 (0-10.6)	38	5	13.2 (4.4-28.1)
Level II total	77	32	41.6 (30.4-53.4)	38	2	5.3 (2.9-13.9)	39	30	76.9 (60.7-88.9)
Level IIA	77	27	35.0 (24.5-46.8)	38	2	5.3 (2.9-13.9)	39	25	64.1 (47.2-78.8)
Level IIB	77	10	13.0 (6.4-22.6)	38	0	0 (0-9.2)	39	10	25.6 (13.0-42.1)
Only other levels		7			0			7	
Contralateral total	30	5	16.7 (5.6-16.7)	28	3	10.7 (2.3-28.2)	2	2	100 (15.8-100)
Level I	20	0	0 (0-16.8)	18	0	0 (0-19.5)	2	0	0 (0-84.2)
Level II total	30	4	13.3 (3.8-30.7)	28	2	7.1 (0.9-23.5)	2	2	100 (15.8-100)
Level IIA	30	4	13.3 (3.8-30.7)	28	2	7.1 (0.9-23.5)	2	2	100 (15.8-100)
Level IIB	30	0	0 (0-11.6)	28	0	0 (0-12.3)	2	0	0 (0-84.2)
Only other levels		01			1			0	

ND, Neck dissection; pN+, pathologically confirmed metastases; cN0, clinical N0 neck; cN+, clinical N+ neck; CI, confidence interval. ^aPercentages relate to the number of patients who underwent dissection of the respective level.

vascular supply leading to shoulder dysfunction (28, 29). Because of the high risks associated with the dissection of levels I and IIB and the time associated with the preparation, the question arises as to in which cases a dissection of these regions is justified and in which cases it can be omitted without impairing the oncological outcome.

The lymphatic drainage of the palatine tonsil and the base of the tongue is mainly directed to the lymph nodes of level II as well as in single cases to the retropharyngeal lymph nodes and to the lymph nodes of level III. The lymph fluid of the posterior wall of the pharynx is also directed to the lymph nodes of levels II and III (30). Numerous studies showed that the frequency of lymph node metastasis of squamous cell carcinomas of the oropharynx in level I was rather low. Especially in patients with clinically N0 cervical lymph node status, only few cases of lymphogenic metastasis to this region are described. In an analysis of 207 patients with oropharyngeal carcinomas, lymph node metastases were found in 7% of elective neck dissections and in 17% of dissections performed in clinical N+ neck in level I (20). Examining 384 patients with carcinomas of the oral cavity, the oropharynx, the larynx, and the hypopharynx retrospectively, metastases were found in level I in 7% (3/58) of the patients with oropharyngeal carcinomas. As in this evaluation neck levels II, III, and IV were identified as the regions with the highest risk of metastasis, the authors recommended SND (II-IV) be performed in patients with oropharyngeal carcinomas and clinical N0 or N1 neck (19). In a prospective examination on the distribution of lymph node metastases in 72 patients with oropharyngeal carcinomas, 5 patients had ipsilateral metastases in level I. In 9% of the patients with clinical N0 neck and in 6% of the patients with clinical N+ status,

metastases were found in level I, so that the authors recommended level I generally be dissected in all patients with oropharyngeal carcinomas (22). Vartanian *et al.* examined 81 patients with oropharyngeal carcinomas and reported about 9 cases of metastasis in the area of level I. They were detected in 18% of the patients with clinical N0 neck and in 8.5% of the cases with clinical N+ neck. Isolated metastases in level I occurred in 5 cases, among them 4 cases with clinical N0 neck. The authors therefore recommended level I be included in the neck dissection even in patients with clinical N0 status (24). In a prospective study of 104 patients with oropharyngeal carcinomas who received 161 neck dissections, none of the patients with clinical N0 neck had metastases in level I. In 10% of the neck dissections in ipsilateral clinical N+ neck, however, metastases were detected, while no metastasis was found histologically in a contralateral clinical N+ neck. Lim *et al.* recommended not performing dissection of level I in patients with clinical N0 neck (31).

In the present evaluation, ipsilateral lymph node metastases were found in 6.5% of all patients with oropharyngeal carcinomas. In none of the cases were metastases detected in a cN0 neck side of level I. It should be the aim to reduce the morbidity related to the extent of surgery and moreover to optimize the efficiency of surgery. Therefore, the presented data support the recommendation stated by the majority of authors to preserve level I in patients with clinically inconspicuous cervical lymph node status. In patients with ipsilaterally clinical N+ neck status, metastases were found in level I in 12.8% of the cases; hence in these cases, dissection of level I seems to be justified.

Although the lymphatic drainage of the oropharynx is directed to lymph nodes in levels II and III, level IIB seems

to be only rarely affected. In a prospective evaluation of 44 patients with carcinomas of the oropharynx and the oral cavity, a rate of occult metastasis in level IIB of 2.1% was found (32). Chone *et al.* who performed a retrospective analysis of 51 patients with different carcinomas of the upper aerodigestive tract, found metastases in level IIB in 1 out of 6 patients with oropharyngeal carcinoma; this patient had a clinical N+ neck and metastases in other neck levels as well (33). In a prospective investigation of 74 patients with carcinomas of the head and neck, none of 15 patients with oropharyngeal carcinomas had metastases in level IIB (34). Lee *et al.* examined 51 patients with oropharyngeal carcinomas. In none of the 36 neck dissection specimens of 21 patients with clinical N0 neck were metastases in level IIB found. In the 30 patients with clinical N+ neck, however, metastases were detected histologically in 7 out of 54 neck dissection specimens that were located on the contralateral, clinically inconspicuous neck side in 2 cases (9). A further investigation analyzing specimens of 26 neck dissections published in the same year revealed lymph node metastases in level IIB in 20% of patients with clinical N0 neck and in 50% of patients with clinical N+ neck (18). In 2007, a prospective multicenter study with 297 patients with head and neck carcinomas revealed 1 metastasis in clinical N0 neck and 1 metastasis in clinical N+ neck in level IIB among 32 patients with oropharyngeal carcinomas (35). In another prospective analysis of 114 patients with squamous cell carcinomas of the head and neck, metastatic spread to level IIB was diagnosed in 3 out of 17 patients with carcinoma of the oropharynx (10).

In the present study, in 13% of the patients with oropharyngeal carcinomas, metastases were found in ipsilateral level IIB. The metastatic rate was relatively high (25.6%) in ipsilateral clinical N+ necks, while no metastases were detected in level IIB in cases with clinical N0 neck. Therefore, the recommendation given by numerous authors to preserve level IIB in patients with oropharyngeal carcinomas and clinical N0 neck (9, 33, 34) is supported by the present data. The high metastatic rate of patients with clinical N+ neck, however, confirms the recommendation given by Chone *et al.* (33) to always dissect level IIB in these cases.

As a limitation of the significance of the present study, it must be considered that not all patients underwent bilateral surgery and a broad spectrum of different types of neck dissection had been performed. This aspect leads to a work-up bias. As not all patients underwent contralateral surgery and level I was not included in the neck dissection in all cases, an underestimation of the metastatic frequency must be expected related to the total number of patients. Moreover, the 95% CIs calculated for all metastatic rates are often rather high because of the low number of cases.

However, the relatively high rate of lymph node metastasis in levels I and IIB in patients with clinically N+

neck justifies dissection of these levels in patients with oropharyngeal carcinomas in order to achieve an optimal oncological result. On the other hand, the present data show that metastases from N0 oropharyngeal cancer rarely occur in levels I and IIB and therefore support the recommendation of preserving levels I and IIB in patients with clinical N0 neck. This may improve functional outcome and postoperative quality of life and, moreover, leads to a reduced operation time without risking oncological safety.

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