Prospective Study on Neck Dissection after Primary Chemoradiation Therapy in Stage IV Pharyngeal Cancer

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Abstract. *Background: Definitive chemoradiation is a well-established option in the treatment of locally advanced squamous cell carcinoma of the head and neck. The intention of this study was to evaluate its efficacy on cervical lymph node metastases in a prospective study after a standardized protocol for chemoradiation (CRT) and histopathological evaluation, respectively. Patients and Methods: The data of 25 patients (10 oropharynx, 15 hypopharynx) who received planned neck dissection after definitive chemoradiation for UICC stage IV carcinomas of the pharynx were analyzed. All patients were sonomorphologically staged positive for lymph nodes (3 patients: N1; 2 patients N2a; 7 patients N2b; 9 patients N2c and 4 patients N3). A neck dissection was carried out 8.9±1.5 weeks (range 6-13) post treatment. The specimens obtained from the different neck levels were histologically examined for viable tumour cells. Results: Local control was achieved in 100% of all patients on endoscopy 9 weeks after the chemoradiation. In 14/25 patients (56%), still viable tumour tissue was found in the neck dissection (ND) specimen. Only one of these 14 patients (7%) was deemed suspicious for residual lymphadenopathy from clinical and diagnostic findings at re-staging after chemoradiation, the others were staged yN0. Postsurgical complications occurred in six patients (24%) such as bleeding and prolonged wound healing in one patient each and functional deficits in an additional four patients. One patient developed a scar recurrence seven months after surgery. Conclusion: Based on these findings, the ultimate efficacy of primary CRT should not be judged 8-10 weeks after the treatment. Therefore planned neck dissection should be performed no earlier than 12 weeks after primary CRT.*

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The treatment of advanced squamous cell carcinoma of the oro- and hypopharynx has changed substantially during the last two decades. Surgery was the treatment of choice until the late 1980s. Potential drawbacks of radical surgery are extended soft tissue and bone defects with a need for reconstructive surgery including pedicled flaps, which often leads to a compromised function of the pharyngeal structures. Definitive chemoradiation has meanwhile become the standard of care for the treatment of locally advanced squamous cell carcinomas of the head and neck as reasonable alternative to surgical resection in most parts of the world since oncological results are equivalent for both methods (1-3). However, organ preservation and retained function are major benefits for the multimodal treatment approach.

Despite the enormous advances in radiotherapy treatment planning and execution of intensity-modulated radiotherapy (IMRT), 3-D conformal and inverse treatment planning and image-guided radiotherapy (IGRT), nodal tumour control is still a problem of major importance (4-6). Sufficient local control rates are often accompanied by uncontrolled nodal disease. One reason for this is the fact that large lymphadenopathies are generally considered to be radioresistant since they carry hypoxic or necrotic subvolumes of tumour cells. Thus surviving tumour stem cells of nodes in partial remission will ultimately lead to regional failures. This was the background for launching this small prospective study in order to evaluate elective neck dissection as a tool for the detection and ultimately also treatment of persisting subclinical nodal disease and for monitoring peri- and postoperative complications. Patients were treated according to a multicenter trial (ARO 04-01) in locally advanced oro- and hypopharyngeal cancer, which compares hyperfractionated accelerated radiotherapy (HART) up to 72 Gy in six weeks plus additive chemotherapy with mitomycin C /5-fluorouracil (5-FU) in the standard arm *versus cis*-platinum/5-FU in the experimental arm (C-HART). All patients analysed in this study received standardised chemoradiation (CRT) according to the afore-mentioned protocol, as well as a histopathological evaluation performed according a standard evaluation described by Sapundzhiev and co-workers (7).

Table I. *Data of the 25 patients who received planned neck dissection with segmentation of pre-therapeutically and post-therapeutically suspected lymphnodes and histologically proven metastases according to the neck level. The tumoural stages of each patient, lateralization and position are presented. For each neck side pretherapeutical distribution of the neck levels and histological findings in the specimen are presented.*

Patient	Staging	Grading	Localisation of the primary	Before radiochemotherapy		After radiochemotherapy				Histology score
				Sono-positive neck level		Sono-positive neck level		Neck level with vital metastases		
				Ipsilateral	Contralateral	Ipsilateral	Contralateral	Ipsilateral	Contralateral	
927	T4N2aM0	G3	OR	II	none	none	none	II	no ND	4
937	T3N1M0	G3	BTR, cm	II-IV	I	none	none	III	none	3
939	T3N2cM0	G2	OL	II-IV	II	none	none	IV	none	3
941	T4N3M0	G2	VGE	I-II	I-II	none	none	none	none	1
956	T2N3M0	G2	HR	II-V	none	none	none	III	none	2
1018	T4N2cM0	G2	HR	II, III	II	none	none	II/III	none	2
1029	T4N3M0	G3	HL	II/III	II	none	none	none	no ND	1
1047	T2N2bM0	G2	HL	I-III	none	none	none	II	no ND	3
1131	T2N3M0	G2	PPWR	II-IV	II, III	none	none	scar (4)	II (2)	2, 4
1148	T2N2aM0	G2	OR	II, III	none	none	none	IV	none	4
1151	T4N2cM0	G2	BTL	II, III	II	none	none	II	none	2
1157	T3N2cM0	G2	HL	III	none	none	none	none	none	1
1153	T4N2cM0	G2	HR	II	I, V	II	II	III	none	4
1207	T4N2bM0	G3-4	OL	II, III	none	II	none	none	no ND	1
1250	T2N2cM0	G3	HR	II, III	II, III	none	none	none	none	1
1270	T3N2bM1	G2	HR	II, III	none	II	none	none	none	0
1290	T4N2cM0	G2	HR	II	III	none	none	none	none	1
1317	T2N1M0	G3	HR	II	none	none	none	IV	no ND	4
1329	T3N2cM0	G2	HL	II-IV	II, III	none	none	none	none	1
1300	T4N2bM0	G2	PPW	II	none	none	none	none	none	1
1337	T4N1M0	G2	HR	III	none	none	none	V	none	3
1342	T4N2cN0	G2	HL	II, III	II, III	none	II	none	none	0
1345	T3N2bM0	G3-4	HR	II, III	none	none	none	none	none	0
1529	T4N2bM0	G2	HL	II, III	none	II,III	none	II, III	no ND	4
1532	T3N2bM0	G2	OR	II, IV	none	none	none	IV	no ND	3

R=Right side; L=left side; cm=crossing the midline; O=oropharynx; H=hypopharynx; BT=base of tongue; PPW=posterior pharyngeal wall; VGE=vallecula glosso-epiglottica; no ND=no neck dissection performed. The histological score shows the highest score found in any of the examined lymph nodes for the given patient.

Patients and Methods

Patient selection. From March 2004 until February 2008, 25 patients (3 female, 22 male; 45±9.2 years, range 38 to 70 years, Table I) with stage IV carcinomas of the oro- and hypopharynx were treated according to the C-HART protocol in a single institution. Ten patients suffered from oropharyngeal and 15 patients from hypopharyngeal squamous cell carcinomas, respectively. Patients with synchronous or metachronous secondary malignancies, distant metastases, previous surgical treatment, age older than 70 years, diabetes mellitus, increased blood pressure, arteriosclerosis, cirrhosis of the liver, hemoglobin <10 g/dl, pregnancy, or who were breast feeding were excluded from the study.

Staging. The extension of the primary tumour and its lymphadenopathies was determined during the initial clinical investigation including panendoscopy. Multiple tumour biopsies were taken for histological classification. The macroscopically visible margins of the carcinoma were marked by tattooing in most cases to allow a comparison of the tumour extension before and after CRT. After completion of the diagnostic procedures, the tumour was classified according to the UICC TNM system (8).

Table II. *Classification of metastatic lymph nodes after CRT.*

Grade	Histological description
0	Tumour-free lymph node without regressive signs
I	Tumour-free lymph node with degenerative changes such as hyalinosis or fibrosis
II	Partial fibrinoid necrosis of the metastatic lymph node
III	Lymph node with parakeratotic tumour cells
IV	Vital lymph node metastases

Imaging. At the time of the first patient visit, high resolution B-mode sonography of the neck was carried out in every patient. The diameters of enlarged suspicious lymph nodes were

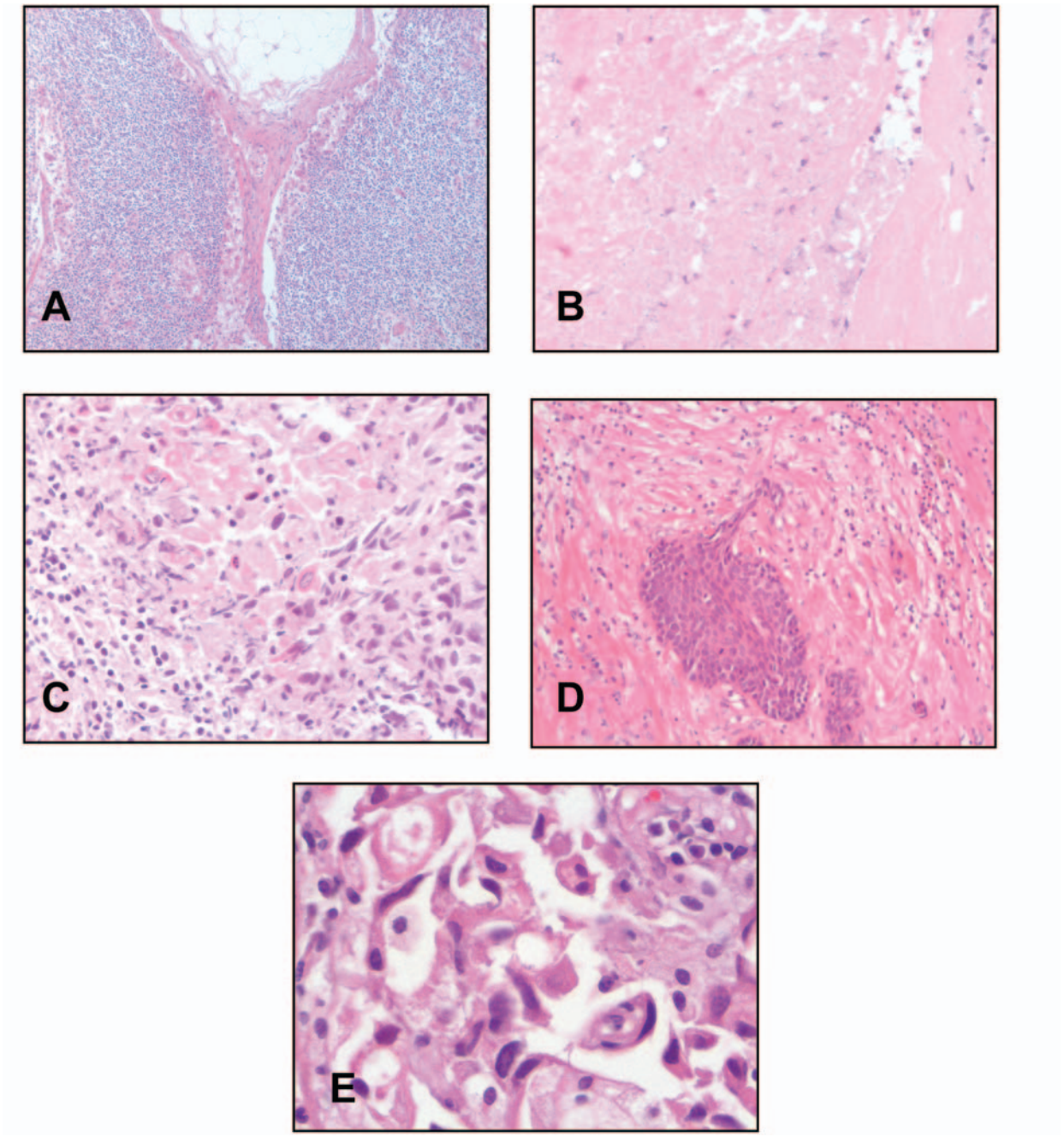

Figure 1. *A, Histopathological slice showing tumour-free lymph node without regressive signs (grade 0); B, tumour-free lymph node with degenerative changes such as hyalinosis or fibrosis (grade I); C, partial fibrinoid necrosis of a metastatic lymph node (grade II); D, lymph node with parakeratotic cells (grade III); E, vital lymph node metastasis (grade IV).*

measured in all three dimensions and documented photographically. Their topographic site was also documented according to the neck level system published by the American Academy of Otolaryngology, Head and Neck Surgery (9). Lymph nodes were considered metastatic with short axial diameter smaller than 7 mm and/or round shape with reduction in the ratio of maximal longitudinal to maximal axial diameter, unclear boundary, or irregular hilar and internal echoes (10, 11). All patients underwent computed tomography (CT) for the primary lesion and lymphadenopathies at the neck and thorax in order to evaluate the depth and extension of tumour infiltration and nodal tumour burden in relationship to the neck. The results of the diagnostic CT-imaging were implemented for the radiation treatment planning.

Table III. *Findings of the pre-therapeutical staging.*

	No. of patients	
	Oropharynx	Hypopharynx
Total	10	15
T stage		
T1	0	0
T2	2	4
T3	3	4
T4	5	7
N stage		
N1	1	2
N2a	2	0
N2b	3	4
N2c	2	7
N3	2	2
G stage		
G1	0	0
G2	7	11
G3	2	3
G3-4	1	1

Chemoradiation (CRT). Patients were treated according to the C-HART protocol (Study Coordinator: Professor Dr. V. Budach, Charité, Berlin, Germany). After concurrent CRT of six weeks, a panendoscopy followed eight weeks later. If no macroscopic tumour was seen at panendoscopy, uni- or bilateral neck dissection (ND) was carried out as selective or modified radical ND related to the pre- and post therapeutical stages of the neck. Before treatment, the patients were randomised to receive either arm A (C-HART with 72 Gy with 5-FU and mitomycin C) or arm B (C-HART with 72 Gy with 5-FU and *cis*-platinum).

All patients underwent dental evaluation and, if necessary, adequate treatment before irradiation. The irradiation technique and fractionation was the same for both treatment arms. Three treatment techniques were allowed, either a classical 3-field technique according to Million, or a CT-based 3-D conformal, or IMRT technique. Patients were immobilized with a dedicated mask system. The first-order target volume consisted of all macroscopic tumour extensions *e.g.* primary lesion and enlarged lymph nodes. This volume was treated by normofractionated 2 Gy/day up to 30 Gy and subsequently hyperfractionated accelerated fractionation of 1.4 Gy *bid* up to 72 Gy total dose. The interfraction intervals were 6-8 hours. The second-order target volume adjacent to the macroscopic tumour extensions carrying a high risk of microscopic spread (regional lymph nodes) was irradiated similarly up to a total dose of 59.4 Gy. The third-order target volume peripheral to the second-order target volume (supra-regional lymph nodes) consisted of lymph nodes with a lower risk of metastases, which were irradiated up to 49.6 Gy. The patients treated in arm A received chemotherapy on the first and sixth week of treatment. On day 1-5, *i.v.* 5-FU of 600 mg/m^2 was applied. On day 5 and 36, mitomycin C was applied at a dose level of 10 mg/m^2 as bolus injection. In arm B, the same 5-FU application was chosen coupled with additional *cis*-platinum at a dose level of 30 mg/m^2 weekly for 6 cycles.

Surgery. After histologically proven complete remission in the pharynx at an average of 9 weeks post CRT, a planned neck dissection was carried out depending on the pre- and post therapeutic status of the neck nodes. Likewise ND was undertaken in 10 and 15 patients with oro- or hypopharyngeal cancer, respectively. ND was carried out 9.3±1.3 weeks (range 6-12 weeks) post-chemoradiation in patients with carcinomas of the oropharynx. Two of the patients with oropharyngeal cancer underwent modified bilateral radical ND, three additional patients had unilateral modified radical ND. One patient had radical ND of the ipsilateral neck while another patient had modified radical ND in combination with a selective neck dissection of the contralateral side of the neck. ND was carried out 8.6±1.7 weeks (range 7-13) post chemoradiation in patients with carcinomas of the hypopharynx. One patient had unilateral radical ND, another received bilateral modified radical ND. Three patients had ipsilateral modified radical ND in combination with a selective ND of the contralateral site. Four patients had unilateral modified radical ND. Two patients were treated with bilateral selective ND and two further patients with unilateral ND, respectively. After ND, special attention was paid to mark the obtained specimen carefully with coloured needles according to their anatomical site of origin relative to the neck levels.

Histopathological evaluation. The tissues were fixed in 10% formalin solution and embedded in paraffin. Serial sections of the specimen of 6 μm thickness were stained in H&E and periodic acid Schiff (PAS) for histological evaluation. Immunohistochemistry was performed according to the standard biotin-avidin complex (ABC-) peroxidase method with diaminobenzidine. A broad-range cytokeratine antibody (CK MNF 116; DAKO, Hamburg, Germany) was used as chromogen. For each specimen, the total number of lymph nodes and their topographic relation to the neck levels were documented. In each ND specimen, tumour-involved and tumour-free lymph nodes were compared with the neck status before treatment. Histopathological changes in metastatic lymph nodes after CRT were analysed according to the classification described by Sapundzhiev and co-workers (7) and grouped into five stages as shown in Table II and Figure 1.

Grades II-IV contain viable tumour tissue and were considered as regional failures of the CRT protocol. Lymph nodes staged 0 or I were classified as nodal control.

Results

Pre- and postoperative staging. The results of the preoperative staging procedures and the post CRT ND findings for the oro- and hypopharyngeal sites are shown in Tables III and IV. No patient had distant metastasis at the time of initial presentation. Control panendoscopy and re-biopsy of the primary tumours showed total tumour regression in all patients 9 weeks after primary CRT.

Oropharynx. Post-therapeutically, one suspicious lymph node was detected in level II of the ipsilateral side in one patient. All other neck levels of the ipsi- and contralateral side were considered to be free of disease sonomorphologically. Planned neck dissection was performed in 10 patients. Histomorphological examination of the neck dissection

Table IV. *Sonographical and histological findings after CRT.*

	Number of positive lymph nodes			
	Oropharynx		Hypopharynx	
	Ipsilateral	Contralateral	Ipsilateral	Contralateral
Sonography				
Neck level				
I	1	2	3	1
II	20	10	12	5
III	9	2	24	9
IV	0	0	0	0
V	0	0	0	1
VI	0	0	0	0
Histology				
Neck level				
I	0	0	0	0
II	2	0	3	0
III	0	0	0	0
IV	4	4	3	1
V	0	0	0	0
VI	0	0	0	0
Histology score				
0	0		3	
1	3		5	
2	2		2	
3	3		2	
4	2		2	

specimens showed grade I in 3 patients, grade II in 2 patients, grade III in 3 patient, and grade IV in 2 patients. These local failures of CRT were found in one patient in neck level II and III, respectively. In 2 patients vital tumoural tissue was found in level IV of the ipsilateral side whereas 1 patient had a grade II lymph node in Level II of the contralateral side.

Hypopharynx. One patient had suspicious lymph nodes in level II unilaterally and another patient bilaterally after chemoradiation. A third patient had suspicious lymph nodes in level II and III post-therapeutically. The patient with the unilateral lymph-node of level II was staged tumour free histologically, in the patient where metastases could be suspected bilaterally by sonography, a grade 4 node was detected in level III. Grade IV metastases were confirmed in level II and III of the third patient. The histological analysis of the neck dissection specimens were grade 0 in 3 patients, grade I in 5 patients, grade II in 3 patients and grade III in two patients. Grade IV was found in another four patients. Three patients had vital tumour cells in level II and III, respectively, two patients had tumoural tissue in level IV and one patient in level V on the ipsilateral side. The number of pre- and postoperative lymph node findings are summarised in Table V.

Table V. *Number of lymph nodes (LN) dissected in relation to sonomorphologically suspect LN and LN with incomplete response to CRT.*

	Neck level					
	I	II	III	IV	V	Total
Total number of LN	29	163	179	118	48	537
LN with incomplete response*	0	8	5	2	1	16
Sonopositive LN						
Before CRT	13	51	36	0	1	72
After CRT	0	6	1	1	0	8

*Additionally one piece of scar with grade 4.

Postoperative complications. A venous bleeding 5 hours postoperatively was encountered in a patient who received a radical ND for N3-metastasis infiltrating the cervical vessels and sternocleidomastoid muscle. It was managed by reoperation and ligation of the vessel. Severe wound healing with wound dehiscence was observed in another patient suffering from a T4N3M0 carcinoma of the glossoepiglottic fold that needed repetitive plastic reconstructive surgeries including pedicled and free mucocutaneous flaps. Functional deficits, such as weakness and chronic pain of the accessory nerve occurred in 4 patients. Only one and two of these patients had radical or modified radical ND, respectively, with preservation of the accessory nerve. The fourth patient was treated with a selective ND of levels II-IV. In the fifth patient suffering from a T2N3M0 carcinoma of the posterior pharyngeal wall, a recurrence occurred in the cervical scar of the ND seven months after surgery. Overall, postsurgical complications which compromised quality of life were encountered in 25% (5/25) of all patients.

Suspicious lymph nodes were predominantly found in levels II (30 oropharynx, 17 hypopharynx) and III (11 oropharynx, 33 hypopharynx). After the execution of planned NDs for stage II to IV pharyngeal cancer, residual disease was histologically confirmed in 56% (14/25) of all patients indicating insufficient nodal control at the prescribed total dose level of 72 Gy

Discussion

Cancer of the oro- and hypopharynx represent approximately 12% and 4%, respectively, of all head and neck malignancies, most of which are of squamous cell histology (12-14). More than 50% of pharyngeal cancer patients are diagnosed with neck node metastases (14-16). Neck node metastases are one of the major factors carrying a negative prognosis and compromise overall survival (14). Therapeutic strategies in locally advanced oro- and hypopharyngeal cancer patients have changed considerably during the last

decades. Surgery as standard of care until the late eighties of the last century with local control rates in the range 70-90% has been gradually replaced by multimodal treatment strategies (14, 15, 17, 18). However, oncological surgery often resulted in large tissue defects, loss of organ function and ultimately compromised quality of life, which in many cases demanded sophisticated reconstructive surgery. Definitive CRT evolved as an alternative to radical surgery and is currently considered the standard of care for locally advanced head and neck cancer of the pharynx (12, 19, 20). The overall survival rates in locally advanced cases are similar to those treated with surgery alone. CRT in many instances allows organ preservation and retainment of its function (14, 18, 21-25). Although CRT can control the primary tumour in a high percentage of cases, still no reliable diagnostic measure is available to differentiate viable tumour tissue from inflammatory disease and scar formation. The aim of the present study was to evaluate the response rates of lymph node metastases of UICC stage IV oro- and hypopharyngeal carcinomas to definitive CRT.

The knowledge of the pathways for metastatic spread to predefined neck node levels is the basis for selective ND (12, 16, 17, 26-30). Depending on the site of the primary lesion, a characteristic pattern of lymphatic spread can be observed. The typical lymphatic pathways are confirmed in this study by means of pretherapeutic staging. In this study, definitive CRT showed excellent control for the well perfused primary lesions but less efficacy in the lower perfused neck node metastases (31, 32). Radiobiologically, large neck nodes do often carry areas of tumour cell hypoxia or necrosis, which upregulate tumour resistance against ionising irradiation by means of the well-known oxygen effect (31, 32). The majority of tumour cells are not directly killed by ionizing irradiation but are blocked at the interphase of the cell cycle. They ultimately die when entering the S-phase of one of the next cell cycle divisions. Therefore, ultimate efficacy of CRT should not be judged 8-10 weeks post-treatment.

Salvage surgery for persisting neck nodes or planned ND for subclinical disease was generally recommended 6-8 weeks after treatment since some surgeons reported a more difficult preparation of anatomical layers with the onset of radiation fibrosis after time intervals of more than 8 weeks. More recent reports claim intervals up to 12 weeks as also feasible from the surgical point of view in terms of preparation and postoperative wound healing. In the present study, the mean time interval between the end of CRT and planned ND was 9.3±1.3 weeks (oropharynx) and 8.6±1.7 weeks (hypopharynx). Still viable tumour cells persisting after 8-12 weeks post-chemoradiation indicate relative radioresistance of the tumour, *e.g.* due to tumour hypoxia, and lead to further tumour progression. There are several studies with a wide variation of 4-12 weeks of the interval between the end of CRT and planned ND. But considering the option of positron-emission tomography (PET)-CT after CRT, the interval should be 12 weeks (33-35).

Metastatic tumour spread originating from the primary tumour or regional lymph nodes can occur at any time during CRT. The well-known pathways of lymphatic drainage are not only modified by surgical interventions but also by chemoradiation, leading to peculiar patterns of lymphatic spread to unusual neck levels. Mabanta and co-workers (36) found neck recurrences in levels which were initially free of disease in 15% of cases. Histological work-up in this study confirmed the above findings for the development of atypical lymphatic neck drainage after CRT. Viable tumour cells were mainly found in level II followed by level III and IV in this study. At planned ND, 4 patients had lymph node metastases at neck levels III, IV and V, which had been staged by sonography and CT as being disease free before start of treatment Potential explanations for this phenomenon are false-negative diagnosis due to subclinical nodal micrometastases, atypical lymphatic spread of tumour cells from the primary tumour due to previous CRT and secondary dissemination from involved neck metastases (37, 38).

A clinical response evaluation by means of inspection and palpation of the neck post CRT is often of only limited diagnostic value. Standard imaging methods of the neck are magnetic resonance imaging (MRI), CT and B-mode sonography. MRI and CT scans show exact site and extension of cervical tumours and lymph nodes (39). B-mode sonography is little time and resource consuming but in expert hands can yield superior results compared with other imaging techniques (36). Subclinical nodal disease cannot usually be detected until macroscopic neck recurrences are evident. In 107 patients, Boysen and co-workers (40) observed viable tumour tissue in the neck in 5/23 patients without palpable lymph nodes and in 39/65 patients with residual palpable nodes after CRT. Brizel and co-workers (41) reported higher overall and tumour-free survival rates in patients with N2 and N3 necks (77% *versus* 53%, and 75% *versus* 53%) after planned modified radical ND following CRT. B-mode sonography plays an important role during the follow-up of head and neck cancer patients, in particular after surgical treatment and/or definitive CRT in order to detect neck recurrences at the earliest stage (42). If recurrences are still locally confined, a salvage neck dissection or neck revision still carries a curative potential (37). A drawback for sonographic evaluation after CRT in the neck are changes at the level of soft tissues such as fibrosis, edema and lack of differentiation of anatomical landmarks (sternocleidomastoid muscle, internal jugular vein, carotid artery) (43, 44). These changes are expressed quantitatively at different stages in many patients and compromise the predictive value of the investigations.

There is a conflicting body of evidence indicating both treatment strategies with planned ND and a simple surveillance policy to be adequate (33, 45-49). Sapundzhiev

and co-workers (7) found a high incidence of histologically positive lymph nodes (7/17) after definitive CRT in patients with stage IV oropharyngeal cancer. Nouraei and co-workers (50) reported residual viable neck disease in 39% after CRT in patients with stage IV head and neck squamous cell carcinoma. McHam and co-workers (33) found viable tumour cells in the neck dissection specimen in 15/63 (24%) patients after CRT. Hitchcock and co-workers (51) report histologically positive residual disease in 22/41 (53.7%) patients who underwent definitive radiotherapy with or without cisplatin-based chemotherapy for squamous cell carcinoma of the base of the tongue. These findings are confirmed in the current study where after histopathological examination of the neck dissection specimens, tumoural tissue was confirmed in 6/15 patients (40%) with oropharyngeal carcinoma and in 8/16 patients (54%) with carcinoma of the hypopharynx.

Brown and co-workers (52) reported a rate of 13% for prolonged wound healing disorders in all cases of neck surgery. A previous high-dose radiation therapy to the neck considerably increases the rate of postoperative complications after ND by a factor of 5 (53, 54). The hazards involved herein comprise a higher vulnerability of large vessels leading to ruptures of the carotid artery at worst, impaired hemostasis and an increased risk for wound infections and dehiscences. In this study, one patient suffered from prolonged wound dehiscence that had to be covered with several pedicled and free flaps after intensive conservative care of the wounds. Another patient had a postoperative venous bleeding requiring ligation of the vessel five hours after surgery. No carotid ruptures occurred in this study. Four patients complained of functional deficits because of 11th-nerve syndrome after CRT with 72 Gy followed by a planned ND, which showed 16% of all patients to have functional deficits because of nervous lesions or scar formation in the current study. The 11th-nerve syndrome reduces quality of life significantly (55). Nahum and co-workers (56) also found signs of lesions of the accessory nerve after ND in up to 60% of patients who underwent radical neck dissection. Functional impairment of the shoulder can be reduced by physical training of the scapulohumeral girdle muscles. This procedure aims at recovering passive motion and avoids joint fibrosis (57). Fistula of the thoracic duct occurs in about 1-2% of all patients who undergo radical neck dissection (58).

Conclusion

With planned ND, subclinical residual nodal disease was detected in 56% (14/25) of showing a patients regression grade II-IV (according to Sapundziev and co-workers (7)) indicating insufficient nodal control 8 weeks after C-HART. Only one of these 14 patients (7%) at re-staging after CRT who had sonomorphologically suspicious lymph nodes was this confirmed histologically. In another patient, sonographic and histological findings were positive, but the levels of these suspected and real metastases differed from each other. In comparison to the discussed data, the complication rate in this study is of a minor dimension (16% 11th-nerve syndrome, 4% wound healing disorders, 4% postoperative bleeding). Because of the radiobiological mechanisms that are the basis for the effect of radiotherapy, the ultimate efficacy of CRT should not be judged 8-10 weeks after the treatment. This is the main reason why planned ND should be performed at about 12 weeks after primary CRT.

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