Original Article

Primary and adjuvant intensity-modulated radiotherapy in oropharyngeal carcinoma patients from a single institution

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ABSTRACT

Background: To retrospectively access outcome, adverse events and prognostic factors in oropharyngeal carcinoma (OPC) patients treated with intensity-modulated radiotherapy (IMRT).

Methods: Ninety-eight OPC patients were treated between 2000 and 2015. Thirty-three patients received definitive and 65 adjuvant radiotherapy. Seventy-one percent had simultaneous chemotherapy. Patients were systematically followed up (mean 114 months, range 19–197 months). Statistical analysis used Kaplan–Meier method, Cox regression analysis, and log-rank test. Adverse events were classified according to common toxicity criteria version (CTCAE) 4.03.

Results: The 1-, 5-, and 10-year overall survival rates in the adjuvant vs. definitive cohort were 90.8% vs. 66.7%, 67.4% vs. 33.1%, and 57.7% vs. 16.5%. Survival in the adjuvant cohort was significantly longer than in the definitive cohort ($P < 0.00005$). Patients <65 years had a significantly longer survival than older patients. Locoregional tumor control rates after 1-, 5-, and 10 years in the adjuvant vs. definitive cohort were 90.2% vs. 66.7%, 82.2% vs 45.4%, and 72.1% vs. 30.3%. Locoregional tumor control in the adjuvant cohort was significantly longer than in the definite cohort ($P < 0.005$). Distant metastases were diagnosed in 20.4% of all patients. Most patients had mild CTCAE grade 1 and 2 adverse events and mild late adverse events including xerostomia, dysphagia, and lymphedema.

Conclusion: Intensity-modulated radiotherapy for OPC is an important part of the treatment algorithm alone and in particular after surgery while the additional benefits of chemotherapy might be age dependent. Despite advanced tumor stages, nearly half of our patients were alive in the long term. The majority of patients had relatively mild chronic adverse events.

KEY WORDS: Chemoradiation, head and neck cancer, HNSCC, IMRT, intensity-modulated radiotherapy, OPC, OPSCC, oropharyngeal cancer, radiochemotherapy, radiotherapy

INTRODUCTION

In 2016, 1103 women and 3445 men were diagnosed with oropharyngeal cancers (OPC) in Germany.[1] The mean age at diagnosis in oral cavity and pharyngeal cancers was 66 in women and 63 in men.[2] Men were more often diagnosed with UICC stage IV oral cavity or pharyngeal cancers than women (60% versus 47%).[2] The 10-year survival in oral cavity and pharyngeal cancers reported by the Robert Koch Institute (a major federal health agency) in 2016 in Germany was 42% in women and 28% in men.[2] Risk factors were mainly alcohol consumption and smoking.[3,4] Furthermore, increased risks are seen in low economic status and poor dental hygiene.[3] In the last decades, human papilloma virus (HPV)-associated OPC prevalence increased from 40.5% before 2000 up to 72.2% between 2005 and 2009.[5] Treatment approaches include surgery only, surgery and postoperative radio (chemo)therapy as well as definitive radio (chemo)therapy, dependent on disease and patient characteristics. The German Cancer Research Center was one of the first centers worldwide, implementing intensity-modulated radiotherapy (IMRT) as a standard of care. Aim of this analysis was to access the long-term outcome, adverse events, and prognostic factors in a cohort of 98 consecutive patients treated with IMRT for OPC.

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METHODS

Patients' characteristics: At the time patients were treated, human papilloma virus testing was not standard and therefore not performed in our patients. Further patients' characteristics are found in Table 1.

Radiation treatment: The median radiotherapy dose in the definitive (postoperative) cohort was 57.6 Gy (54.0 Gy) on the lymphatic drainage and median 70.4 Gy (66.0 Gy) as a mainly simultaneous integrated boost (SIB) to the primary tumor (bed) and pathologic lymph nodes (bed). Treatment was mainly performed with a Siemens LINAC in step-and-shoot IMRT using median nine beams on five days a week and in the definitive (postoperative) cohort median 32 (30) fractions for a median total radiotherapy time span of 43 (43) days.

Systemic therapy: Simultaneous chemotherapy was applied in 90.9% (61.5%) of patients in the definitive (postoperative) cohort. The most commonly used regimes were cisplatin 40 mg/m2 body surface area weekly (62.9%) or carboplatin 70 mg/m2 body surface area in combination with 5-FU 600 mg/m2 body surface area in weeks 1 and 5 (31.4%). Other regimens used were 5-FU mono in one patient and cetuximab weekly in three patients. Ten patients (30.3%) in the definitive

Table 1: Patients' characteristics

	Definite RT		Postoperative RT		Total	
	n	%	*n*	%	*n*	%
Age at initial diagnosis						
<65 years	24	72.7	55	84.6	79	80.6
≥65 years	9	27.3	10	15.4	19	19.4
Gender						
Female	9	27.3	11	16.9	20	20.4
Male	24	72.7	54	83.1	78	79.6
Residual tumor following surgery						
R0			36	55.4	36	55.4
R1			28	43.1	28	43.1
R2			1	1.5	1	1.5
Grading						
G1	2	7.1	2	3.1	4	4.3
G2	18	64.3	35	54.7	53	57.6
G3	7	25.0	27	42.2	34	37.0
G4	1	3.6	0	0	1	1.1
T stage						
T1	2	6.1	18	27.7	20	20.4
T2	1	3	27	41.5	28	28.6
T3	5	15.2	12	18.5	17	17.3
T4	24	72.7	8	12.3	32	32.7
Not available	1	3	0	0	1	1
N stage						
N0	4	12.1	10	15.4	14	14.3
N1	2	6.1	11	16.9	13	13.3
N2a	0	0	7	10.8	7	7.1
N2b	10	30.3	30	46.2	40	40.8
N2c	14	42.4	7	10.8	21	21.4
N3	3	9.1	0	0	3	3.1
M stage						
M0	33	33.7	65	66.3	98	100
M1	0	0	0	0	0	0
AJCC/UICC stage						
I	0	0	4	6.2	4	4.1
II	0	0	3	4.6	3	3.1
III	3	9.1	14	21.5	17	17.3
IV	30	90.9	44	67.7	74	75.5
Induction chemotherapy						
No	23	69.7	63	96.9	86	87.8
Yes	10	30.3	2	3.1	12	12.2
Simultaneous chemotherapy						
No	3	9.1	25	38.5	28	28.6
Yes	30	90.9	40	61.5	70	71.4
Alcohol consumption						
No	6	18.2	26	40.6	32	33
Yes	27	81.8	38	59.4	65	67
Smoking history						
No	3	9.1	15	23.4	18	18.6
Yes	30	90.9	49	76.6	79	81.4

cohort had induction chemotherapy (docetaxel/cisplatin/5-FU), two patients (3.1%) in the adjuvant cohort.

Statistical design and classifications: The primary endpoint of this retrospective analysis was overall survival (OS), and the secondary endpoints local control (LC) and adverse events (AE). Time estimates refer to the start of radiotherapy. LC was defined as the absence of local tumor progression including all cases of stable disease (less than 50% tumor mass reduction), partial remission (tumor mass reduction of at least 50%), and complete remission (requiring no detectable disease). Survival analyses (due to limited patient count, a multivariate analysis was performed in the postoperative cohort only) were carried out with I.B.M. SPSS 25 using Kaplan–Meier estimation, log-rank test, and Cox regression analysis (backward stepwise). A *P* value of 0.05 was considered statistically significant. AE were classified according to the common toxicity criteria for adverse events (CTCAE) version 4.03. The first follow-up examination including magnetic resonance imaging (MRI) or computed tomography (CT) of the neck was performed 6–8 weeks after finishing radiotherapy and every three months thereafter in the first year, every six months in the second year, and once a year thereafter. The local ethics committee approved the analysis (Heidelberg, Germany, protocol number S170/2012). Date: 24.05.2012.

RESULTS

Patients' characteristics: Between 2000 and 2015, 98 consecutive patients with a median age of 57 years and the diagnosis of oropharyngeal squamous cell carcinoma (OPSCC) were treated with definitive ($n = 33$) or postoperative ($n = 65$) radio (chemo)therapy at our research center.

Survival and tumor control: At the time of data analysis of this study, 44 (44.9%) patients were still alive. Of the deceased patients, one died during radiotherapy. Median follow-up for the whole cohort was 46 months (1–216 months). Median OS for all patients was 100 months and the 1-, 3-, 5-, and 10-year OS rates were 82.7%, 66.3%, 55.8%, and 44.3%, respectively [Figure 1].

Median OS in the primary/definitive radiotherapy cohort was 29 months and the 1-, 3-, 5-, and 10-year OS rates were 66.7%, 39.4%, 33.1%, and 16.5%. Median OS in the postoperative cohort was 172 months and the 1-, 3-, 5-, and 10-year OS rates were 90.8%, 80.0%, 67.4%, and 57.7%, respectively. Thus, survival in the postoperative cohort was significantly longer than in the definitive cohort ($P < 0.00005$). Recurrent disease was diagnosed in 28 patients (primary radiotherapy $n = 15$ and postoperative radiotherapy $n = 13$) after median 9.5 months. Median LC in the primary cohort was 56 months and the 1-, 3-, 5-, and 10-year LC rates were 71.3%, 54.3%, 46.5%, and 31.0%, respectively [Figure 2].

Median LC in the postoperative cohort was not reached and the 1-, 3-, 5-, and 10-year LC rates were 90.5%, 85.1%, 82.7%,

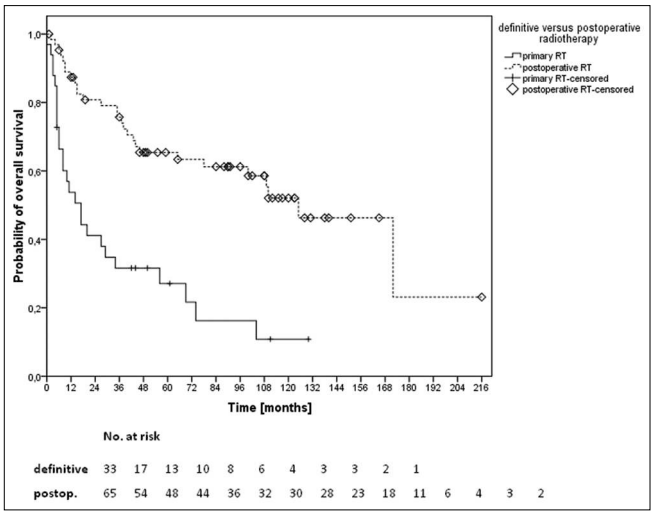

Figure 1: Overall survival of 98 patients treated with either definitive ($n = 33$) or postoperative ($n = 65$) radio (chemo)therapy for oropharyngeal squamous cell carcinoma

and 73.6%, respectively. Patients within the postoperative cohort had a significantly longer median LC ($P < 0.000$). Distant metastases (DM) were diagnosed in 20 patients of the whole cohort [Figure 3]. In the definitive cohort eight patients (24.4%) and in the postoperative cohort 12 patients (18.5%) developed distant metastases during follow-up.

Patients with N0–1 disease had significantly less common DM compared to N2–3 disease ($P = 0.035$). DM developed primarily within the first two years and after median eight months (range, 2–125 months). The 3-, 5-, and 10-year DM-free survival (DMFS) rates were 77.4% each time. Patients with N0–1 disease had a significantly better DMFS compared to N2–3 disease ($P = 0.035$).

Prognostic and predictive factors for patient overall survival

In univariate analyses, patients receiving simultaneous chemotherapy had a significantly shorter survival than those, without simultaneous chemotherapy ($P = 0.018$). Median OS was 51 months with simultaneous chemotherapy and 172 months without simultaneous chemotherapy. Patients < 65 years had a negative impact from simultaneous chemotherapy ($P = 0.022$), while patients >/= 65 years did not show this age dependence ($P = 0.92$). The type of simultaneous chemotherapy had borderline significance for OS [$P = 0.055$, Figure 4].

Furthermore, induction chemotherapy resulted in shorter OS ($P = 0.02$): median OS 32 months with versus 116 months without induction chemotherapy. T stage had a significant impact on OS: median OS in stage T1 was 172 months compared to 116 months in stage T3 and 26 months in stage T4. Median OS in T2 was not reached. In the primary radiotherapy cohort, patients with stage T1–T3 tumors lived significantly longer than those with T4 tumors ($P = 0.02$). In the postoperative cohort, no difference in OS dependent on T stage was seen ($P = 0.65$). Patients with N0–1 stage did not

have a statistically significantly longer OS than those with N2–3 disease (130 months versus 43 months, $P = 0.1$). Further parameters are found in Table 2.

In multivariate analysis of the postoperative cohort, none of the analyzed parameters including the induction and simultaneous chemotherapy were prognostic or predictive of OS [Table 3]. However, older age >57 years ($P = 0.064$) and higher AJCC/UICC tumor stage ($P = 0.078$) showed a strong trend towards worse outcome.

Prognostic and predictive factors for local tumor control

In univariate analysis, prognostic/predictive factors for improved LC were primary surgery ($P < 0.000$), no history of alcohol consumption ($P = 0.003$), and lower tumor stages I–III versus IV disease ($P = 0.045$). Prognostic/predictive factors for worse LC were a primary tumor in the lateral or dorsal pharyngeal wall ($P = 0.009$) and induction chemotherapy ($P = 0.034$). However, parameters including gender ($P = 0.519$), primary tumor location in the tonsillar fossa ($P = 0.853$), primary tumor location in the base of the tongue ($P = 0.176$) and soft palate ($P = 0.499$) as well as simultaneous chemotherapy ($P = 0.113$), history of smoking ($P = 0.085$), histological tumor grading ($P = 0.875$), age < versus >65 years ($P = 0.122$), and residual tumor status ($P = 0.939$) did not reach statistical significance.

In multivariate analysis of the postoperative cohort, the only parameter prognostic/predictive of LC was no alcohol consumption ($P = 0.035$) [Table 4].

Table 2: Further univariate analysis results

Parameter	*P*
Age <65 years versus ≥65 years	0.047*
Gender male versus female	0.33
Grading G1-2 versus G3-4	0.96
Residual disease R0 versus R+	0.42
Alcohol consumption yes versus no	0.058
Smoking history yes versus no	0.69

Log-rank test, *significance *P*<0.05 on prognostic factors for overall survival

Table 3: Multivariate analysis of the postoperative cohort on parameters for overall survival

Parameter	*P*
Age <65 years versus ≥65 years	0.28
Age< or >median age of 57 years	0.064
Gender male versus female	0.61
Residual disease R0 versus R+	0.733
Alcohol consumption yes versus no	0.126
Smoking history yes versus no	0.477
Tumor stage T1-2 versus T3-4	0.901
Tumor stage UICC 1-3 versus 4	0.078
Simultaneous chemotherapy	0.358

Cox regression analysis, backwards stepwise, *Significance *P*<0.05

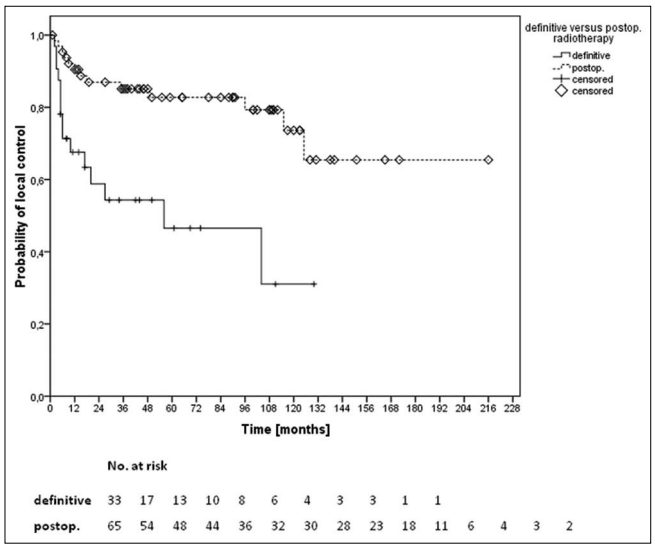

Figure 2: Local control of 98 patients treated with either definitive ($n = 33$) or postoperative ($n = 65$) radio (chemo)therapy for oropharyngeal squamous cell carcinoma

Acute and chronic adverse events

No relevant IMRT treatment interruptions were documented. Common acute AE attributable to radiotherapy and partially to chemotherapy were xerostomia (83.0%), reduced general condition (38.3%), and reduced nutritional state (28.7%). A prophylactic percutaneous endoscopic gastrostomy feeding tube (PEG) was placed in 81.4% of patients, and 54.3% of patients had documented weight loss. However, 83.3% regained their body weight. Three months after radiotherapy, 29.5% of patients still had a PEG in situ. In total 8.6% of patients receiving simultaneous chemotherapy did not complete their chemotherapy due to acute AE. One patient receiving platin-based chemotherapy developed repeated venous thrombosis during chemotherapy, one other patient had persistent thrombocytopenia, and one patient showed persistent thrombocyto- and leucopenia. One patient receiving cetuximab developed severe skin and mucous membrane reactions resulting in a discontinuation of cetuximab. In one patient, 5-FU monotherapy had to be canceled due to persistent

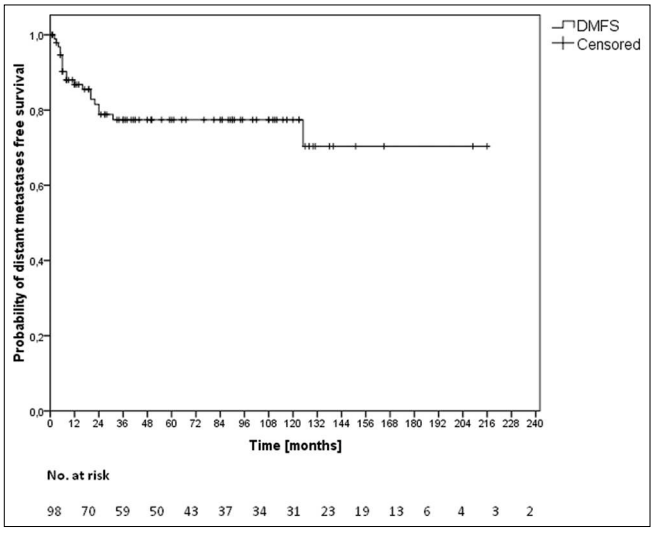

Figure 3: Distant metastases free survival of 98 patients treated radio (chemo)therapy for oropharyngeal squamous cell carcinoma

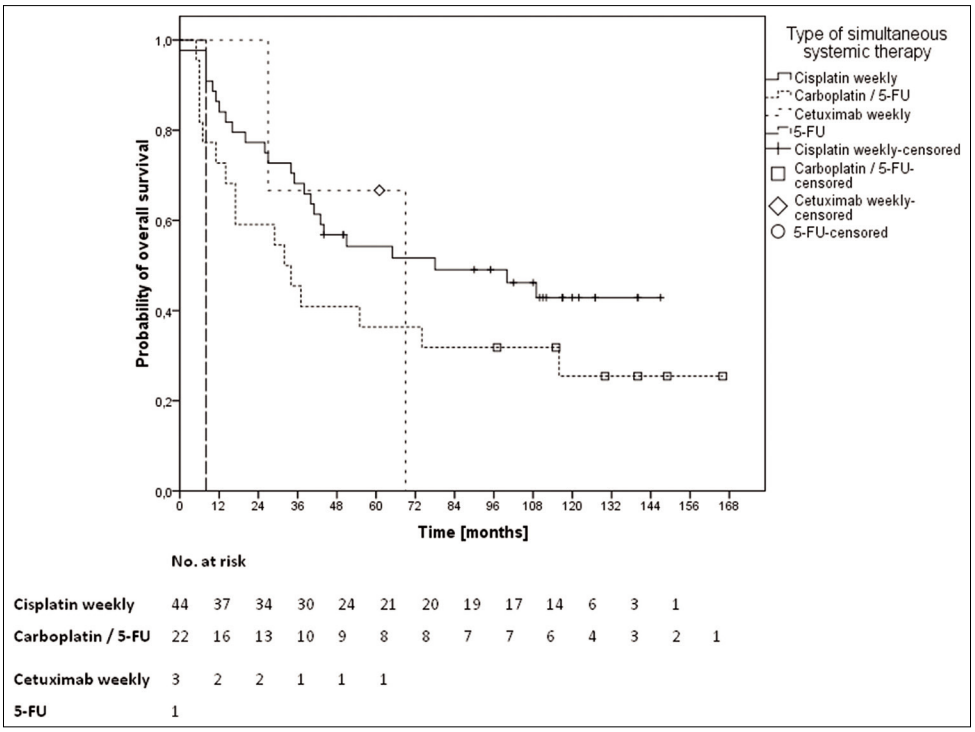

Figure 4: Overall survival stratified by different types of simultaneous systemic therapy for oropharyngeal squamous cell carcinoma (cisplatin weekly $n = 44$, carboplatin/5-FU $n = 22$, Cetuximab $n = 3$, 5-FU only $n = 1$, borderline significance $P = 0.055$)

Table 4: Multivariate analysis of the postoperative cohort on parameters for local control

Parameter	*P*
Age < or >median age of 57 years	0.947
Gender male versus female	0.957
Residual disease R0 versus R+	0.275
Alcohol consumption yes versus no	0.035*
Smoking history yes versus no	0.986
Tumor stage T1-2 versus T3-4	0.818
Tumor stage UICC 1-3 versus 4	0.813
Simultaneous chemotherapy	0.212

Cox regression analysis, backwards stepwise, *Significance $P<0.05$

cytopenia and high liver laboratory values. Most of the acute AE improved over time. However, especially xerostomia grade 1 and 2 as well as trismus, sensation deficits in the head and neck area and lymph edema did not subside markedly over time. Furthermore, 29.5% of patients needed a PEG and 16.7% had significant weight loss more than three months after treatment was finished. Further acute and chronic AE are found in Tables 5 and 6.

DISCUSSION

We analyzed a cohort of 98 consecutive patients with OPSCC who were treated relatively uniformly at our research center between 2000 and 2015. It was our aim to retrospectively access the long-term treatment outcomes and AE in our patients. All but nine patients had more than six years of follow-up. Important to us, all consecutively treated patients with OPSCC and exclusion of distant metastases during initial staging were included in the analysis and no patients were excluded based on compliance, performance status, or comorbidities. Therefore, our cohort represents a real-life collective of all stage M0 OPSCC patients seen in daily clinic.

The tumor register Munich reported 2021 an observed general 5- and 10-year OS in OPC patients of 56.5% and 43.3%, respectively.[6] The National Cancer Institute reported 2021 a relative general 5-year OS of 71.2% for the years 2011 to 2017.[7] Therefore, our results are with a 5- and 10-year OS of 55.8% and 44.3%, respectively, within the previously reported general survival rates in OPC. The postoperative cohort had a 3-year OS of 80% and was comparable to prior reports. For example, Daly *et al.*[8] reported a 3-year OS of 83% in their analysis on IMRT in OPC. In contrast, our definitive cohort had a 3-year OS of 39.4% and performed poorer than expected. Lee *et al.*[9] reported 2006 a 3-year OS of 91% in 41 patients treated with IMRT for advanced OPC. However, in the report by Daly *et al.*,[8] tumor stage T4 was a significant predictor of poorer OS. Also, the tumor register Munich reported reductions in 5- and 10-year survival from 70.9% and 59.8%, respectively, to 34.8% and 23.1% when patients were diagnosed with tumor stages T3 or T4 versus T1.[6] The difference between our cohort and mentioned prior reports might be explained by the relatively high number of patients with advanced stage T4 (72.7% in our cohort compared to 29% in the study by Daly *et al.*[8]) and/or >/= stage N2c (51.5%) as well as 90.9% AJCC/UICC stage IV disease and high number of smokers (90.9%) in our definitive cohort. Furthermore, time estimations are based on the start of radiotherapy and we included one patient (3%) who did not finish his treatment in the definitive cohort.

Table 5: Acute adverse events from radio (chemo) therapy (*n*=97)

Acute adverse events	*n*	%	Acute adverse events	*n*	%	Acute adverse events	*n*	%
Reduced general condition	38	39,2	Dermatitis			Dysosmia		
Reduced nutritional condition	28	28,9	Grade 0	27	27,8	Yes	12	12,4
Xerostomia			Grade 1	18	18,6	Anosmia	2	2,1
Grade 0	17	17,5	Grade 2	40	41,2	Nausea	30	30,9
Grade 1	38	39,2	Grade 3	11	11,3	Vomiting	17	17,5
Grade 2	22	22,7	n.a.	2	2,1	Oropharyngeal candidiasis	24	24,7
Grade 3	10	10,3	Lymph edema			Hypacusis	13	13,4
not available	11	11,3	Grade 0	57	58,8	Tinnitus	5	5,2
Mucositis			Grade 1	11	11,3	Fatigue	26	26,8
Grade 0	26	26,8	Grade 2	8	8,2	Hoarseness	13	13,4
Grade 1	16	16,5	Grade 3	8	8,2	Reduced shoulder-arm mobility	12	12,4
Grade 2	26	26,8	n.a.	14	14,4	Facial nerve paresis	7	7,2
Grade 3	24	24,7	Pain			Vertigo	5	5,2
not available	6	6,2	Mild	25	25,8	Dysphonia	9	9,3
Trismus			Moderate	8	8,2	Headache	6	6,2
Grade 0	79	81,4	Intense	11	11,3	Dyspnea	5	5,2
Grade 1	3	3,1	n.a.	19	19,6	Reduced visual acuity	3	3,1
Grade 2	1	1,0	Dysgeusia			Hypoglossal nerve paresis	4	4,1
Grade 3	2	2,1	Grade 0	10	10,3	Abducent nerve paresis	1	1,0
not available	13	13,4	Grade 1	26	26,8	Sensation deficits head and neck area	7	7,2
Dysphagia			Grade 2	32	32,9	Muscle cramps	1	1,0
Grade 0	16	16,5	Ageusia	26	26,8	Neck stiffness	1	1,0
Grade 1	29	29,9	n.a.	4	4,1	Dysosmia		
Grade 2	13	13,4				Yes	12	12,4
Grade 3	23	23,7				Anosmia	2	2,1
not available	17	17,5				Nausea	30	30,9

Table 6: Chronic adverse events from radio (chemo) therapy (*n*=78)

Chronic adverse events	*n*	%	Chronic adverse events	*n*	%	Chronic adverse events	*n*	%
Reduced general condition	22	28,2	Dermatitis			Dysosmia		
Reduced nutritional condition	13	16,7	Grade 0	73	93,6	Yes	10	12,8
Xerostomia			Grade 1	4	5,1	Anosmia	1	1,3
Grade 0	12	15,4	Grade 2	0	0	Nausea	3	3,8
Grade 1	35	44,9	Grade 3	0	0	Vomiting	2	2,6
Grade 2	20	25,6	n.a.	1	1,3	Oropharyngeal candidiasis	2	2,6
Grade 3	5	6,4	Lymph edema			Hypacusis	11	14,1
not available	6	7,7	Grade 0	37	47,4	Tinnitus	5	6,4
Mucositis			Grade 1	15	19,2	Fatigue	17	21,8
Grade 0	62	79,5	Grade 2	10	12,8	Hoarseness	9	11,5
Grade 1	11	14,1	Grade 3	2	2,6	Reduced shoulder-arm mobility	11	14,1
Grade 2	0	0	n.a.	14	17,9	Facial nerve paresis	4	5,1
Grade 3	0	0	Pain			Vertigo	2	2,6
not available	5	6,4	Mild	12	15,4	Dysphonia	2	2,6
Trismus			Moderate	5	6,4	Headache	3	3,8
Grade 0	60	76,9	Intense	3	3,8	Dyspnea	1	1,3
Grade 1	10	12,8	n.a.	7	9,0	Reduced visual acuity	0	0
Grade 2	5	6,4	Dysgeusia			Hypoglossal nerve paresis	2	3,8
Grade 3	0	0	Grade 0	29	37,2	Abducent nerve paresis	0	0
not available	3	3,8	Grade 1	41	52,6	Sensation deficits head and neck area	8	10,3
Dysphagia			Grade 2	5	6,4	Muscle cramps	3	3,8
Grade 0	35	44,9	Ageusia	3	3,8	Neck stiffness	2	2,6
Grade 1	28	35,9	n.a.	0	0	Dysosmia		
Grade 2	8	10,3	Dermatitis			Yes	10	12,8
Grade 3	1	1,3	Grade 0	73	93,6	Anosmia	1	1,3
not available	6	7,7	Grade 1	4	5,1	Nausea	3	3,8

In our analysis, more men than women as well as patients younger than 65 years were diagnosed with OPC, which is consistent with prior reports.[10] Furthermore, patients < 65 years showed an improved OS in our study. This is also consistent with prior reports; for example, the tumor register Munich reported a decreased observed 5- and 10-year survival in patients older than 50 years and further reductions in observed survival after 60 and 70 years of age.[6] The benefit of simultaneous chemotherapy as well as decreasing positive effects with increase in age was proven in several trials. For example, Bourhis *et al.*[11] reported a reduction of the chemotherapy benefits with increase in age of patients in altered fractionation regimes. In our definitive (postoperative) cohort, 90.9% (61.5%) of patients

received simultaneous chemotherapy. However, simultaneous chemotherapy did not improve OS in our patients. The exact reason for this unexpected finding is not finally known. It might be due to very advanced disease stages (in the whole cohort 75.5% stage IV disease) or a combination of it with smoking and/or additional comorbidities in a relatively small cohort. For example, the high rate of smoking in our patients (in the whole cohort 81.4%) might have negatively impacted on the OS, as shown by Hoff *et al*.[12] However, unfavorable or biased patient selection for additional chemotherapy, comorbidity complications after finishing treatment or statistical variance might have also played roles in this finding.

The locoregional recurrence rates in OPC reported by Röösli *et al*.[13] in 2009 after a median follow-up of 49 and 72 months were 35% and 53%, respectively. The 3-year local control reported by Daly *et al*.[8] was 91%. In our cohort, the 3- and 5-year LC rates in the postoperative setting were 84.6% and 82.2%, respectively, and comparable to prior reports.[13] However, the results in the definitive setting with 3- and 5-year LC rates of 53% and 45.4%, respectively, were lower than previously published, even though Gupta *et al*.[14] reported a comparable 5-year LC after definitive radiochemotherapy of 49% in patients with advanced head and neck cancers.

Looking at the AE, Daly *et al*.[8] reported in their cohort of IMRT for OPC an acute mucositis grade 3 rate of 58%, which was higher than 24.5% in our cohort. Greco *et al*.[15] analyzed the presence of feeding tubes after IMRT for head and neck cancer patients and reported 1- and 5-year rates of 7.1% and 4.8%, respectively. In our cohort, 29.5% of patients had a PEG for more than three months. In general, swallowing disturbances might be reduced by optimization of the dose applied to the swallowing musculature.[16,17] In our study, 54.3% of patients had documented weight loss as acute AE, which is lower than in the trial by Nutting *et al*.,[18] where 80% of patients treated with IMRT had weight loss grades 1–3. Furthermore, 71.7% and 76.9% of our patients reported acute and late xerostomia, respectively. In the trial by Nutting *et al*.,[18] 100% of patients treated with IMRT had acute and late xerostomia. Furthermore, 38.8% and 44.9% of patients in our cohort reported the lower xerostomia grade 1 acute and late AE, respectively, compared to 70% and 83% having grade 2 and above acute and late xerostomia, respectively, and only 30% and 17% acute and late grade 1 xerostomia, respectively, in the trial by Nutting *et al*.[18]

Limitations of this analysis are the retrospective design and the slightly different systemic therapy regimens. Furthermore, a multivariate analysis on risk factors was performed for the postoperative cohort only due to a relatively low patient number in the definitive cohort. However, the inherent inhomogeneous characteristics of a consecutive patient cohort mirrors the real-life outcome which partially may balance the shortcomings.

CONCLUSION

Intensity-modulated radiotherapy for OPC is feasible and safe in the long term. IMRT remains an important part of the treatment for OPC in the definitive and postoperative setting. Even being diagnosed with advanced tumor stages, nearly half of our patients were alive in the long term. At the same time, the quality of life is getting increasingly acceptable with the majority of patients not reporting higher grade chronic adverse events.

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Conflicts of interest

There are no conflicts of interest.

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