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The Survival of Head and Neck Carcinoma Patients Depends on Secondary Causes of Death

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Abstract

Purpose: The study aimed to analyse causes of death and differential survival after multimodal treatment of head and neck carcinoma patients. Methods and Materials: Between September 2000 and December 2015, 935 patients received a multimodal treatment of head and neck carcinoma. Of these, 562 patients (60.1%) underwent a resection of the primary tumour and a postoperative radio- or radiochemotherapy and 373 patients (39.9%) received definitive radio- or radiochemotherapy. The median follow-up was 21.0 months (0.5 - 175.4 months). Results: At the endpoint of the investigation, 465 patients (49.7%) were alive. The median survival of all patients was 44.8 months (0.5 - 164.3 months). A total of 470 patients (50.3%) died. The causes of death were divided into five groups: 22 patients (2.4%) died of therapy-associated complications with a median of 2.2 months (1.6 - 3.3 months). The 160 patients (17.1%) with intercurrent death, 117 patients (12.5%) with deaths from locoregional progression with or without metastasis, and 86 patients (9.2%) with deaths from metastasis without locoregional recurrence showed comparable survival curves with a median survival of 13.3 months, 13.6 months, and 14.4 months. Eighty-five patients (9.1%) died from second malignant diseases and controlled treated head and neck carcinomas with a median survival of 34.5 months ($P < 0.001$). Conclusion: Despite a locoregional control and metastasis-free survival of 78.3% patients, only 49.7% of the patients were alive, due to a high rate of intercurrent and second malignant diseases. The short median survival rate is mainly due to the tumours (locoregional and or distant progression) and intercurrent causes of death, with the second malignant diseases leading to death later on.

Keywords

Head and Neck Carcinoma, Radiochemotherapy, Causes of Death

1. Introduction

Multimodal treatment of patients with head and neck carcinoma results in disappointing overall survival rates, despite the substantially better disease-free survival rates in definitive as well as postoperative radiochemotherapy trials. An increased comorbidity of these patients, especially due to smoking and alcohol consumption, is discussed. We analysed our head and neck carcinoma patients multimodally treated with a curative intention from September 2000 to December 2015.

The purpose was to analyse the causes of death and their influence on survival.

2. Methods and Materials

Between September 2000 and December 2015, 935 patients (772 male, 163 female) received a multimodal treatment of head and neck carcinoma. The mean age of the patients was 59.3 years (30.5 - 90.2 years). Of these, 562 patients (60.1%) underwent a resection of the primary tumour and a postoperative radio- or radiochemotherapy and 373 patients (39.9%) received definitive radio- or radiochemotherapy only. After treatment, all patients underwent frequent follow-up examinations with an otolaryngologist and a radiooncologist. The median follow-up was 21.0 months (0.5 - 175.4 months), and the loss to follow-up was 13.3% (124 patients). Patients' characteristics are shown in Table 1. A total of 832 patients (89%) received the treatment primarily, 103 patients (11%) had a recurrence after a history of an initially resected small primary lesion without adjuvant treatment and were multimodal treated at the time of locoregional recurrence without distant metastasis. Sixty-three of the patients (6.7%) completed their irradiation in an untimely manner.

Survival rates were estimated according to the Kaplan-Meier method; differences between groups were assumed by means of the log-rank statistic. For statistical analysis, Microsoft Excel 2008 and SPSS Version 23 were used.

3. Results

At the endpoint of the investigation, 465 patients (49.7%) were alive. The median survival of all patients was 44.8 months (0.5 - 164.3 months). During the investigated interval, 470 patients (50.3%) died. Female patients showed a median survival of 80.3 months whereas male patients had a median survival of 40.3 months ($P < 0.001$) (Figure 1). While patients with postoperative radio-(chemo-)therapy had a median survival of 65.2 months, patients with a definitive treatment had a significantly shorter median survival of 21.7 months ($P < 0.001$) (Figure 2).

Table 1. Patient characteristics.

Gender		
Male	772	82.6%
Female	163	17.4%
Primary Tumour Localisations		
Oropharynx	340	36.4%
Larynx	140	15.0%
Hypopharynx	131	14.0%
Floor of the mouth	120	12.8%
Tongue	53	5.7%
CuP	48	5.1%
Nasopharynx	39	4.2%
Paranasal sinuses	25	2.7%
Salivary glands	19	2.0%
Skin	11	1.2%
Ear canal	5	0.5%
Lip	4	0.4%
UICC Stage		
I	31	3.3%
II	72	7.7%
III	129	13.8%
IVA	656	70.2%
IVB	46	4.9%
IVC	1	0.1%
Primary Tumour Resection		
Without resection	373	39.9%
R0	381	40.7%
R1	181	19.4%

The causes of death were divided into five groups: therapeutic-associated deaths, intercurrent deaths with locoregional and systemic tumour control, deaths due to and after a locoregional recurrence, deaths with distant metastasis and a locoregional controlled tumour, and deaths from a second malignant disease. Twenty-two patients (2.4%) died from therapy-associated complications after a median of 2.2 months (1.6 - 3.3 months) and had a significant lower median survival (Table 2, Figure 3).

The 160 patients (17.1%) with intercurrent deaths, 117 patients (12.5%) with deaths from locoregional progression with or without metastasis, and 86 patients (9.2%) with deaths from metastasis without locoregional recurrence showed comparable survival curves with a median survival of 13.3 months, 13.6 months,

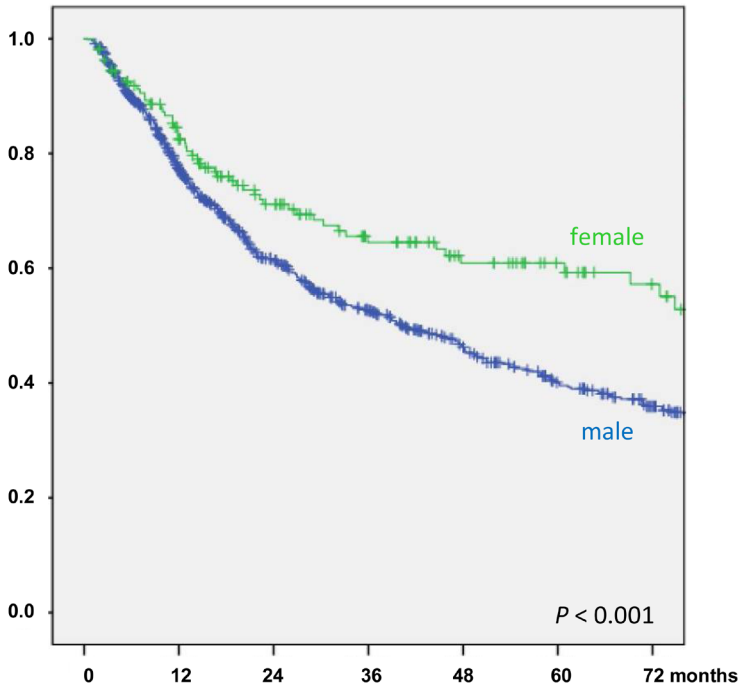

Figure 1. Survival rates (months) of male and female patients.

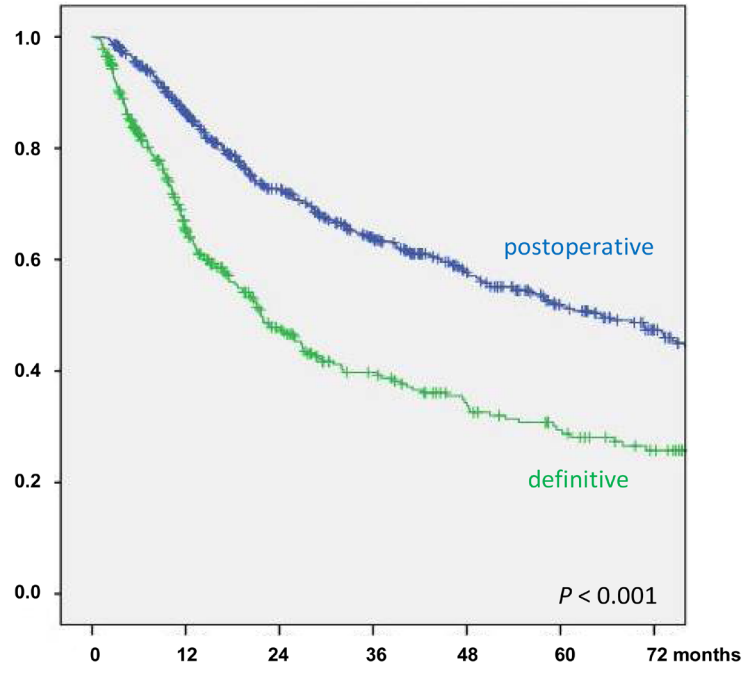

Figure 2. Survival rates (months) of postoperative and definitive treated patients.

and 14.4 months, respectively. Eighty-five patients (9.1%) died from a second malignancy and controlled head and neck carcinoma. They had a significantly longer median survival of 34.5 months ($P < 0.001$). Fifty-one of the 85 (60%) fatal second malignant diseases were lung cancer diseases, 10 patients (12%)

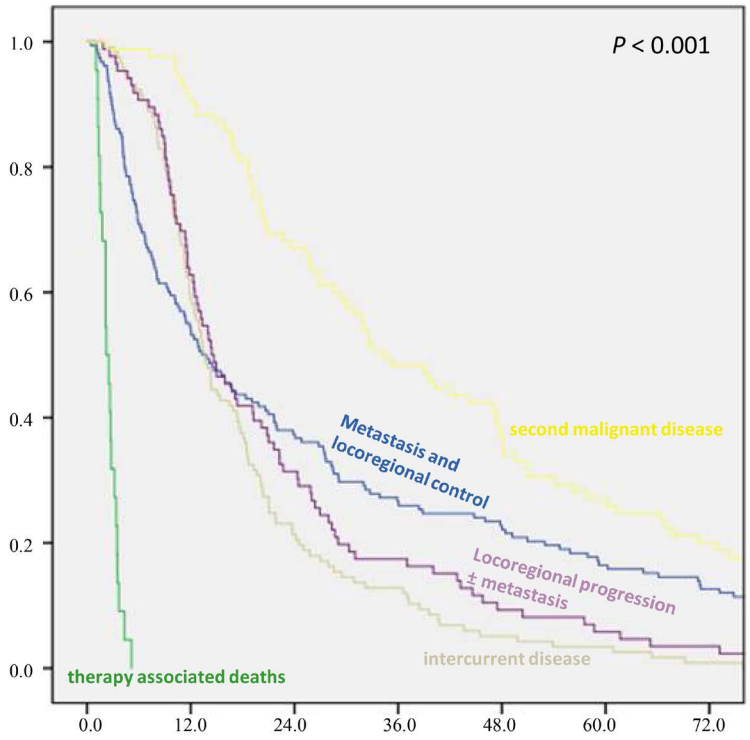

Figure 3. Survival rates depending on the cause of death (green line: therapy-related death, grey: locoregional progression, purple: distant metastasis locoregional control, blue line: intercurrent disease, yellow line: second malignant disease).

Table 2. Survival of patients depending on causes of death.

	n	(%)	Median Survival
All patients	935	100	16.0 months
Deceased patients			
Therapy associated	22	4.7	2.4 months
Intercurrent disease	160	34.0	13.2 months
Locoregional progression ± metastasis	117	24.9	13.6 months
Metastasis and locoregional control	86	18.3	14.6 months
Second malignant disease	85	18.1	34.5 months

suffered from oesophageal carcinoma, and 5 patients (6%) from a second head and neck carcinoma.

4. Discussion

4.1. Locoregional Control Rates

For patients receiving postoperative radio- or radiochemotherapy, locoregional control rates after 2 years were between 46% and 82% [1] [2] and after 5 years were between 36% and 80% [1] [2]. In comparison to this, our patients had lo-

coregional control rates after 2 and 5 years of 86.1% and 80.8%, respectively. The published data of locoregional control rates after definitive radio- or radio-chemotherapy after 2 years, 3 years, and 5 years were 42% - 57% [3] [4], 39% - 52% [3] [4], and 38% - 50%, respectively [4], and in a nonrandomized trial of 90%, after 2 years as well as after 5 years [5]. The own data showed locoregional control rates of 74.0%, 72.6%, and 68.7% after 2, 3, and 5 years, respectively.

4.2. Survival Rates

The published survival rates of postoperative treated patients were 56% - 71% after 2 years [1] [2] and 38% - 53% [1] [2] after 5 years, as well as after definitive treatment of 38% - 60% after 2 years [3] [4], 26% - 37% after 3 years [3] [4], and 24% - 29% after 5 years [4] as well as in a nonrandomized trial of 80%, 58%, and 50% after 2, 3, and 5 years [5]. In our analysis, we found comparable survival rates of 71.8% and 46.6% after 2 years for the postoperative and definitive treated patients as well as 51.1% and 30.1% after 5 years.

Bernier *et al.* described a rate of second malignant diseases after 5 years of 12.5% [2]. We found 145 (15.5%) second malignant diseases after a median follow-up of 21 months; 85 of these 145 (58.6%) second malignant diseases led to patient death. This increased rate could also be an effect of the nonselected patient group.

In comparison to the published trials, we treated an unselected patient population. The median age of our patient group is an average of 5 years older. We treated a larger spectrum of primary tumour localisations, and 381 of 935 (41.7%) patients had exclusion criteria of the mentioned radiochemotherapy trials.

4.3. Causes of Death

One reason for the short survival of these patients could be high comorbidity due to long-term alcohol and nicotine consumption, when 34% of the patients died from intercurrent diseases. These patients did not live longer than patients who died due to the failure of locoregional therapy or exclusively distant disease progression. Patients who survived longer had a high risk of suffering from a second malignant disease with a reduced prognosis.

5. Conclusion

The survival of patients with head and neck carcinoma after definitive or postoperative radio-chemotherapy was lower despite acceptable locoregional control rates of treatment.

Conflict of Interest

All authors declare no conflicts of interest.

References

[1] Cooper, J.S., Pajak, T.F., Forastiere, A.A., *et al.* (2004) Postoperative Concurrent

Radiotherapy and Chemotherapy for High-Risk Squamous-Cell Carcinoma of the Head and Neck. *The New England Journal of Medicine*, **350**, 1945-1952. https://doi.org/10.1056/NEJMoa032646

[2] Bernier, J., Domenge, C., Ozsahin, M., *et al.* (2004) Postoperative Irradiation with or without Concomitant Chemotherapy for Locally Advanced Head and Neck Cancer. *The New England Journal of Medicine*, **350**, 1937-1944. https://doi.org/10.1056/NEJMoa032641

[3] Staar, S., Rudat, V., Stuetzer, H., *et al.* (2001) Intensified Hyperfractionated Accelerated Radiotherapy Limits the Additional Benefit of Simultaneous Chemotherapy—Results of a Multicentric Randomized German Trial in Advanced Head-and-Neck Cancer. *International Journal of Radiation Oncology • Biology • Physics*, **50**, 1161-1171. https://doi.org/10.1016/S0360-3016(01)01544-9

[4] Budach, V., Stuschke, M., Budach, W., *et al.* (2005) Hyperfractionated Accelerated Chemoradiation with Concurrent Fluorouracil-Mitomycin Is More Effective than Dose-Escalated Hyperfractionated Accelerated Radiation Therapy Alone in Locally Advanced Head and Neck Cancer: Final Results of the Radiotherapy Cooperative Clinical Trials Group of the German Cancer Society 95-06 Prospective Randomized Trial. *Journal of Clinical Oncology*, **23**, 1125-1135. https://doi.org/10.1200/JCO.2005.07.010

[5] Adelstein, D.J., Saxton, J.P., Lavertu, P., *et al.* (2002) Maximizing Local Control and Organ Preservation in Stage IV Squamous Cell Head and Neck Cancer with Hyperfractionated Radiation and Concurrent Chemotherapy. *Journal of Clinical Oncology*, **5**, 1405-1410. https://doi.org/10.1200/JCO.2002.20.5.1405