

COMPARISON OF THE EFFECTIVENESS OF OROPHARYNGEAL SQUAMOUS CELL CARCINOMA TREATMENT OVER TWO TIME PERIODS WITH RESPECT TO HPV INCIDENCE

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Abstract

BACKGROUND: Oropharyngeal squamous cell carcinoma (OPSCC) is a heterogenous disease with at least two disease entities. First group of patients are heavy smokers and alcohol abusers and second group of patients is younger without history of smoking and alcohol abuse. The former group is prevalent in Slovenia, while the later group is associated with HPV infection and has a better prognosis for survival. In the world, the second form of the disease has been recognized as an epidemic in recent years, and the number of patients is expected to increase in the coming years. **METHODS:** We retrospectively evaluated the survival of the patients with OPSCC in two separate time periods treated at the Clinic of Otolaryngology Head and Neck Surgery in Maribor, Slovenia. Patients were divided into two groups. Group A encompassed patients treated from 1998 to 2003 and Group B patients treated from 2012 to 2016. **RESULTS:** Overall survival rates for group A and group B were 46% and 45% respectively, while disease specific survival rates were 56% and 62%. In the group A, the subgroup of non surgical treatment modality saw a higher increase in disease specific survival, 22%. Survival rates for the p16+ OPSCC treated surgically and postoperative chemoradiation were 22% higher compared to the p16- patients. **CONCLUSIONS:** Chemotherapy as addition to the postoperative radiation helped to increase the survival in surgical and non-surgical groups compared to the historical group A, also the time to progression of the disease increased from 24 to 42 months.

Introduction

Current evidence point to the fact that oropharyngeal squamous cell carcinoma (OPSCC) is a heterogenous disease, with at least two different disease entities. First group of patients are heavy smokers and alcohol abusers and the second group of patients is younger without history of smoking and alcohol abuse. The former group is prevalent in Slovenia, while the later group is associated with HPV infection. The prognosis for survival in the former group is lower compared to the later set of the patients. The prevalence of HPV infection in Slovenia is between 20 to 30%. In the last decade the modality of treatment also changed in OPSCC. Chemoradiation became the preferred modality, compared to the more traditional approach with surgery and postoperative (chemo)radiation. The increase in survival of patients with OPSCC is attributed to the higher prevalence of the HPV cancer.

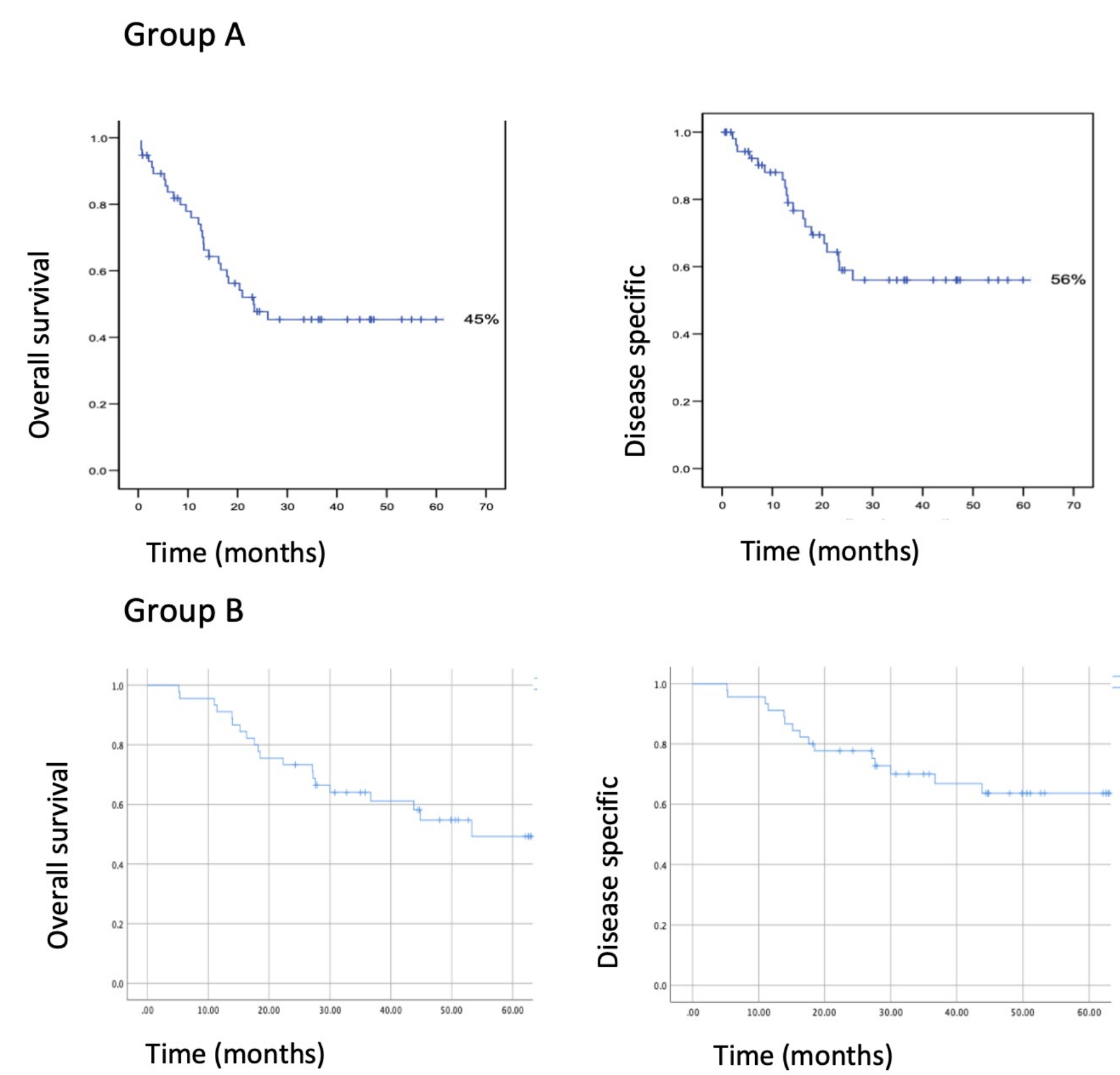
Methods

The medical documentations and National Cancer Registry data of the patients treated for OPSCC in Maribor was reviewed. Patients were divided into two groups. Group A encompassed patients treated from 1998 to 2003 and Group B patients treated from 2012 to 2016. HPV status was determined with p16 staining in group B, while estimation of the prevalence in the historic group was given according to the national study of the HPV+ cancer. In both groups patients were divided into surgical and non-surgical group.

Results

In group A we treated 83 patients with OPSCC. The majority were male (91%, n=76) and 9% (n=7) were female. We treated 69.5% (n=57) primarily with surgery and 30.5% (n=26) with primary radiotherapy. In group B we treated 87 patients with OPSCC. The majority were still male 86%, n=74) and only 14% (n=13) female. We divided patients in group B depending on p16 status in p16- group (N=63) and p16+ (N=41). 46% (N=45) were treated with primary surgery and 54% (N=42) with primary chemoradiation. According to UICC TNC classification we divided tumors into early stage (I and II) and advanced stage (III and IV). In group A 27 patients had early stage tumors (stage I (N=9) and stage II (N=18)), advanced stage tumor had 55 patients (stage III (N=15) and stage IV (N=40)). Regional metastases were present in 83% (n=68) patients, 12 were N1, and 56 N2. 17% (N=14). 17% (N=14) had no regional involvement. In group B 8 patients had early stage disease (stage I (N=2), stage II (N=6)) and 79 patients had advanced disease (stage III (N=10) and stage IV (N=69)). Regional metastases were presend in 85% (N=82), 8 patients had N1, 65 N2 and 9 N3. Overall 5-year survival in group A was 46% and disease specific 56%. Overall survival in group B was 45% and 62% disease specific. Patients treated only with radiation had significantly worse disease specific survival, compared to chemoradiation (20% vs 40%). Contribution of chemotherapy to overall 5-year survival was 20%. (Table 1).

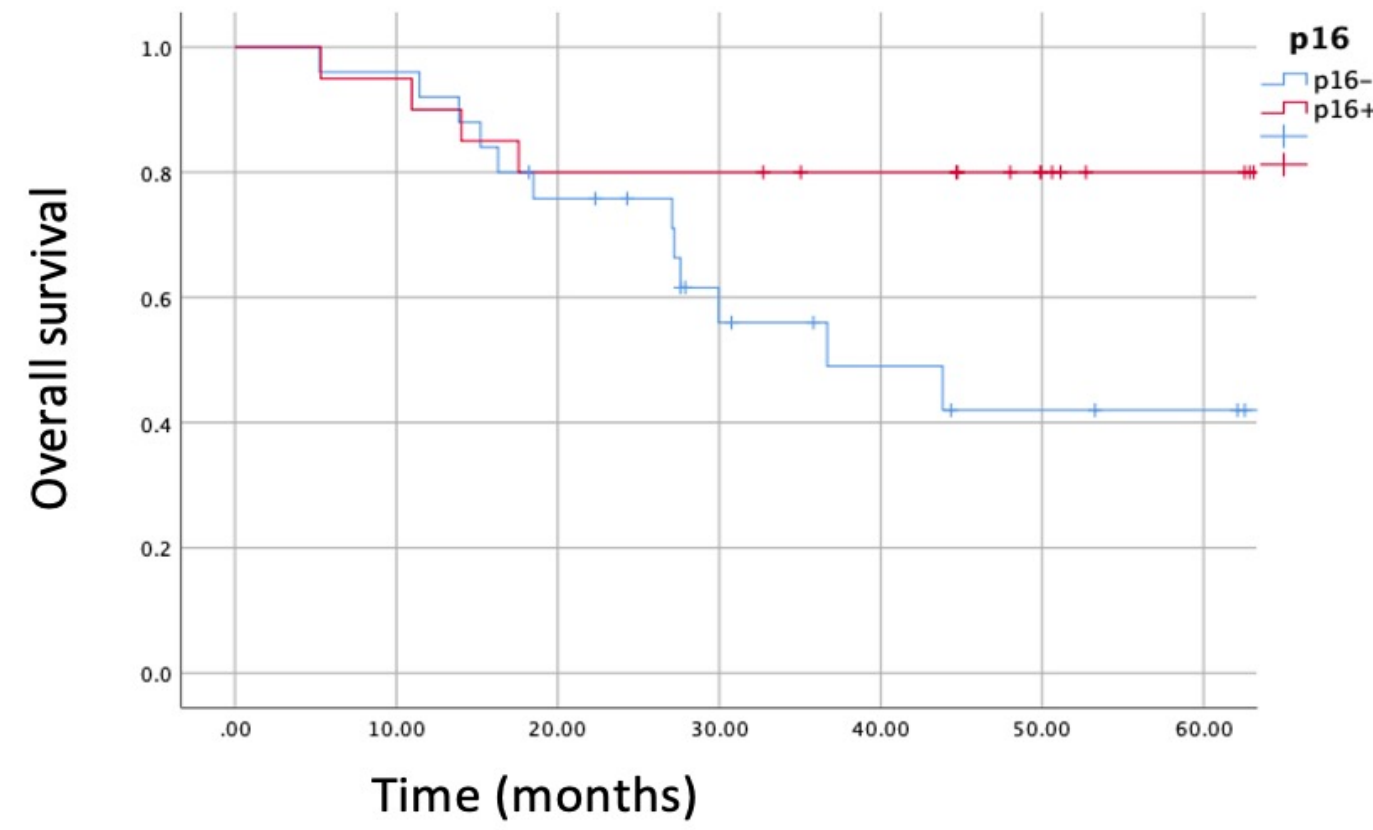
Table1. Group A: Overall and disease specific 5-year survival of patients after combined treatment of OPSCC from 1998-2003, group B: Overall and disease specific 5-year survival of patients after combined treatment of OPSCC from 2012-2016



Patients in group A who were treated primary with surgery and had early OPSCC (stage I and II) had a 100% 5-year overall survival, patients with advanced disease stage III had 48% overall survival and 52% in stage IV. Patients primary treated with radiotherapy had 50% overall survival in early stage (I and II) and 19% in advanced disease (III and IV). Patients in group B who were treated primary with surgery and had early OPSCC (stage I and II) had a 88% 5-year overall survival and patients with advanced disease (stage III and IV) had 58%. Those treated with primary chemoradiation with advanced disease had 38% overall 5-year survival.

For group B we also analysed survival in regard to p16 status. Overall disease specific survival was 48% for p16+ and 40% for p16- tumors (Table 2). Survival for both groups was statistically significantly different (Cox regression p<0.05%). Survival of patients treated primarily with chemoradiation was 44% for p16- tumors and 40% for p16+ tumors. The two groups were not statistically significantly different (p> 0.05).

Table 2. Disease-specific survival of patients with oral pharyngeal cancer treated in the period from 2012 to 2016 according to p16 status.



Conclusion

In the early 20th century, the anti-smoking campaign led to a reduction in tobacco-related head and neck cancer, while at the same time the incidence of oral cancer increased in developed countries (Scandinavia and the US) (1). Particularly in oropharyngeal cancer, it has become clear that in addition to historical factors (smoking and alcohol), HPV is also involved in etiopathogenesis (2). If HPV-related cancer accounted for about 20% of all oropharyngeal cancer cases in the 1980s, this proportion increased to 70% in some countries in 2005 (3) In Slovenia, the incidence of HPV-related oropharyngeal cancer is still significantly lower. A retrospective review found that the proportion of HPV-positive oropharyngeal cancer in patients diagnosed between 2007 and 2008 was 20.2%. Thus, in Slovenia we do not detect a growing trend of OPSCC compared to other HPV-related cancers of the head and neck. The reasons for the different trend compared to other European countries are probably to be found in different sexual habits, preventive behavior and different socio-economic status. Thus, patients with HPV - cancer are mostly male, while the distribution between the sexes in HPV + cancer is more balanced (4). A comparison of the treatment of patients in 1998-2003 and 2012-2016 showed that the addition of chemotherapy to the treatment improved overall survival by 6% and those who were primarily treated with radiotherapy by as much as 20%. Our study showed a better 5-year survival of patients with p16 + cancer, but this percentage is only 8%. Chemotherapy as addition to the postoperative radiation increased survival in surgical and non-surgical groups, compared to the historical group. Therapy de-escalation in patients with HPV+ cancer should be approached with caution not to diminish the positive effect of chemoradiation in surgical and non-surgical arm.

Literature

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