Clinical Research / **Klinik Araştırma**

J Med Updates 2013;3(3):109-115
doi:10.2399/jmu.2013003002

JOURNAL OF medical updates
www.jmedupdates.org

Prognosis in head and neck cancer: the importance of the patient-, and treatment-related factors

Baş boyun kanserlerinde prognoz: Hasta ve tedaviyle ilişkili faktörlerin önemi

Birsen Yücel[1], Mehmet Fuat Eren[1], Ebru Akkaş Atesever[2], Turgut Kaçan[3], Zekiye Hasbek[4], Mehmet Metin Şeker[3]

[1]*Department of Radiation Oncology, Faculty of Medicine, Cumhuriyet University, Sivas, Turkey*
[2]*Department of Radiation Oncology, Dr. Abdurrahman Yurtarslan Ankara Oncology Training and Research Hospital, Ankara, Turkey*
[3]*Department of Medical Oncology, Faculty of Medicine, Cumhuriyet University, Sivas, Turkey*
[4]*Department of Nuclear Medicine, Faculty of Medicine, Cumhuriyet University, Sivas, Turkey*

Abstract

Objective: To investigate the importance of comorbidity, performance status, hemoglobin level, weight loss, interruption of radiotherapy, and mucositis as prognostic factors in head and neck cancer patients.

Methods: Two-hundred and ten patients who were admitted to the Oncology Center of our university between 2006 and 2012, and treated for head and neck cancer were included in the study. Performance status at admission was evaluated according to Eastern Cooperative Oncology Group (ECOG) scoring system. Staging of the disease was based on TNM staging system revised in 2010.

Results: The median follow-up period was 24 (range: 1-134) months. Recurrence was observed in 24% of the patients in a median 11 (range: 3-96) months. Metastasis was observed in 13% of patients, in the median 15 (range: 1-134 months). The 3-year local control, overall survival and disease-free survival rates were 72%, 59%, and 53%, respectively for all patients. The factors affecting the 3-year local control rates in univariate analysis were performance status (p=0.006), weight loss (p=0.002), localization (p=0.003), and stage (p<0.001) of the disease, and perineural invasion (p=0.011). The 3-year overall survival rates were not influenced by comorbidity (p=0.045), performance status (p<0.001), hemoglobin level (p<0.001), weight loss (p<0.001), perineural invasion (p=0.017), lymphovasculer invasion (p=0.022), localization (p=0.007), and stage of the disease (p<0.001), and interruption of radiotherapy (p=0.041). The prognostic factors for the 3-year disease-free survival were comorbidity (p=0.045), hemoglobin level (p<0.001), weight loss (p<0.001), perineural invasion (p=0.017), lymphovascular invasion (p=0.022), localization (p=0.007), and stage of the disease (p<0.001).

Conclusion: Weight loss and perineural invasion for local control; performance status, weight loss, hemoglobin level, and interruption of radiotherapy for overall survival; performance status, weight loss, and hemoglobin level for disease-free survival were found to be independent prognostic factors in multivariate analysis.

Key words: Head and neck cancer, weight loss, hemoglobin.

Özet

Amaç: Bu çalışmanın amacı baş boyun kanserinde prognostik faktör olarak komorbidite, performans durumu, hemoglobin düzeyi, kilo kaybı, radyoterapiye ara verme ve mukozitin öneminin araştırılmasıdır.

Yöntem: Üniversitesimizin Onkoloji Merkezine 2006 ve 2012 tarihleri arasında, baş boyun kanseri tanısı ile tedavi edilen 210 hastanın verileri incelendi. Hastaların performans durumu, hasta başvurusunda Eastern Cooperative Oncology Group (ECOG) skorlama sistemine göre değerlendirildi. Hastalık evresi 2010'da revize edilen TNM evrelemesine göre yapıldı.

Bulgular: Hastalar, medyan 24 (dağılım: 1-134) ay takip edildi. Medyan 11 (dağılım: 3-96) ayda hastaların %24'ünde nüks gelişirken, medyan 15 (dağılım: 1-134) ayda %13'ünde uzak metastaz gelişti. Tüm hastalar için 3 yıllık lokal kontrol %72, 3 yıllık genel sağkalım %59, 3 yıllık hastalıksız sağkalım %53 idi. Tek değişkenli analizde hastaların lokal kontrol oranlarını performans durumu (p=0.006), kilo kaybı (p=0.002), hastalık lokalizasyonu (p=0.003), evre (p<0.001) ve perinöral invazyonun (p=0.011) etkilediği görüldü. Hastaların 3 yıllık genel sağkalımını komorbidite (p=0.045), performans durumu (p<0.001), hemoglobin düzeyi (p<0.001), kilo kaybı (p<0.001), perinöral invazyon (p=0.017), lenfovasküler invazyon (p=0.022), hastalık lokalizasyonu (p=0.007), evre (p¬<0.001), radyoterapiye ara vermek (p=0.041) etkilemekteydi. Komorbidite (p=0.045), hemoglobin düzeyi (p<0.001), kilo kaybı (p<0.001), perinöral invazyon (p=0.017), lenfovasküler invazyon (p=0.022), hastalık lokalizasyonu (p=0.007), evre (p<0.001) ise 3 yıllık hastalıksız sağkalımı için prognostik faktörler oldu.

Sonuç: Çok değişkenli analizde, kilo kaybı ve perinöral invazyon lokal kontrol için; performans durumu, kilo kaybı, hemoglobin düzeyi ve radyoterapiye ara vermek genel sağkalım için; performans durumu, kilo kaybı, hemoglobin düzeyi hastalıksız sağkalım için bağımsız prognostik faktörler olarak belirlendi.

Anahtar sözcükler: Baş boyun kanseri, kilo kaybı, hemoglobin.

Correspondence: Birsen Yücel, MD. Department of Radiation Oncology, Faculty of Medicine, Cumhuriyet University, 58140, Sivas, Turkey.
e-mail: yucelbirsen@yahoo.com

Received: May 11, 2013; **Accepted:** June 19, 2013; **Published online:** January 29, 2014

Online available at:
www.jmedupdates.org
doi:10.2399/jmu.2013003002
QR code:

Head and neck cancers which constitute nearly 6% of all cancers are the sixth most frequently seen type of cancer worldwide with at least 500,000 new cases reported every year.[1] According to the data released by Ege University among 43,134 cancer patients, head and neck cancers rank third in men, and fifth in women with respective incidences of 12.6, and 5.6 percent.[2]

In the management of early stage head and neck cancers local surgery, and radiotherapy (RT) are generally sufficient for cure. Nearly 40% of these patients are diagnosed in the late stages of their disease, and combination therapies including RT, and chemotherapy are required for these patients because of their poor survival rates.[3]

Recognition of prognostic factors guides the clinicians during their therapeutic decision-making process, and in the prediction of survival times, and quality of lives of their patients. In head and neck surgeries, apart from disease-related factors as stage, histopathologic features, perineural and/or lymphovascular invasion, genetic characteristics of the tumor invasion, patient-, and treatment-related factors effect prognosis of the disease. For example, patient-related prognostic factors include comorbidities, and performance status, and disease-, while treatment-related factors consist of hemoglobin level, weight loss, interruption of radiotherapy, and development of mucositis.

In this study, the importance of prognostic factors as comorbidities, performance status, hemoglobin levels, weight loss, interruption of radiotherapy, and mucositis in head and neck cancers has been investigated.

Materials and Methods

Data of the patient who had consulted to the Oncology Center of Training and Research Hospital of Cumhuriyet University Faculty of Medicine between 2006 and 2012 with the diagnosis of head and neck surgery were retrospectively examined.

Performance status of the patients was evaluated using Eastern Cooperative Oncology Group (ECOG) scoring system. Staging was performed based on TNM staging system revised in 2010. Hemoglobin values determined at admission were used later for the evaluation of survival rates. Weight loss was defined as a 5% decrease from baseline body weights of the patients. Differences in body weights of the patients between the start and end of the treatment were estimated for the cases who received RT, and chemoradiotherapy (CRT), while for surgical patients relevant data were retrieved from medical records of the patients.

Radiotherapies of all patients were performed using a dual energy linear accelerator (Varian Clinac DHX; Varian Medical Systems, Inc., Palo Alto, CA, USA) and 6 MV X ray, and 9-12 MeV electron energy. Three-dimensional reconstructions of RT were made using ECLIPS version 8.6 software (Varian Medical Systems, Inc., Palo Alto, CA, USA) program. Exposure field of RT was construed according to the disease stage, and location of the tumor. For adjuvant RT or CRT daily fractional doses of 1.8-2 Gy were delivered amounting to a total dose of 60-66 Gy. For definitive RT or CRT a total dose of 70-74 Gy was applied. Two different CRT protocols were applied as cisplatin 40 mg/m^2 or cisplatin 25 mg/m^2+ docetaxel 25 mg/m^2. Adverse effects of RT, and CRT were evaluated every week of the treatment according to the RTOG/EORTC toxicity criteria. From the year 2009, the patients started to receive oral alimentation solution, glutamine and amifostine adjusted to the doses of RT directed at by the salivary glands.

Statistical Analysis

A statistical package program (SPSS v. 15.0; SPSS Inc., Chicago, IL, USA) was employed for frequency and T-tests, while survival rates were estimated using Kaplan-Meier analysis. For the evaluation of independent factors influential on survival rates, a multivariate Cox regression analysis was used. A p value <0.005 was accepted as statistically significant.

Results

In this study, data of 210 patients (males, n=176, 84%, and females, n=34, 16%) were analyzed. Median ages of the whole study population, male, and female patients were 56 (range: 19-86), 58 (range: 19-86), and 46 (range: 19-80) years, respectively. Initial diagnosis of the female patients was made at an earlier age with a statistically significant difference between genders (p=0.002).

Patients aged <65 (n=146, 69%) or ≥65 (n=64, 31%) years. Laryngeal cancer was the most frequently seen (n=90, 43%) cancer type. Parotid gland cancer (10/13 patients, 77%) was the most common cancer among salivary gland tumors. Mostly squamous cell carcinoma (n=184, 88%) was seen. Other histopathological types of head and neck tumors (total n, n=26, 12%) encountered were as follows: mucoepidermoid carcinoma (n=7), adenoid cystic carcinoma (n=10), mucosal malign melanoma (n=4), soft tissue tumor (n=2), acinar cell carcinoma (n=2), and salivary duct carcinoma (n=1). Demographic data and treatment results of the patients are shown in Table 1.

Median RT dose of 60 Gy was delivered to patients on adjuvant RT or CRT, while median RT dose of 70 Gy was

used for patients under definitive RT of CRT. Cisplatin (n=58, 73%) or cisplatin + docetaxel (n=21, 27%) chemotherapy protocols were applied for a total of 79 patients on CRT.

A hundred and two patients (49%) lost weight during therapies, while in 35 of 181 patients under RT, and CRT, RT was deferred for 5 days or longer due to adverse effects of the therapy. As adverse effects grade 1-2 (n=92; 51%) and 3-4 oral mucositis (n=50, 28%) developed in a total of 142 (78%) patients. Also grade 1-2 (n=126, 70%), and 3-4 (n=15) dysphagia evolved in a total of 141 (78%) patients, while 123 (59%) patients began to complain of nausea, and vomiting. During therapy n=132 (63%) patients used glutamine for the treatment of oral mucositis, and 117 (56%) patients received oral alimentation solution,

The patients were followed up for 1-134 (median: 24) months. At median 11 (range: 3-96) months 51 (24%) patients developed recurrences, while in 28 (13%) patients distant metastases evolved at median 15 (range: 1-134) months.

For all patients average 3-year local disease control rate was 72 percent. In a univariate analysis, local control rates were affected by performance status (p=0.006), weight loss (p=0.002), location (p=0.003), and stage of disease (p<0.001) and perineural invasion (PNI) (p=0.011). In a multivariate analysis, weight loss (p=0.034, HR=3.01, 95% CI=1.08-8.36), and PNI (p=0.52, HR=2.57, 95% CI=0.99-6.68) were determined as independent prognostic factors.

For all patients 3-year overall survival rate was 59 percent. Three-year overall survival rate of the patients was affected by the presence of comorbidities (p=0.045), ECOG performance status (p<0.001), hemoglobin levels (p<0.001), weight loss (p<0.001), PNI (p=0.017), lymphovascular invasion (LVI) (p=0.022), location (p=0.007), and stage of the disease (p<0.001), and interruption of RT (p=0.041). For 3-year overall survival rates ECOG performance status (p=0.040, HR=3.52, 95% CI=1.06-11.70), weight loss (p=0.025, HR=6.21, 95% CI=1.26-30.54), hemoglobin level (p=0.012, HR=5.59, 95% CI=1.46-21.42) and interruption of RT (p=0.006, HR=4.73, 95% CI=1.55-14.40) were determined as independent prognostic factors.

For all patients median 3-year disease-free survival rate was 53 percent. Presence of a comorbidity (p=0.045), hemoglobin levels (p<0.001), weight loss (p<0.001), PNI (p=0.017), LVI (p=0.022), location (p=0.007), and stage of the disease (p<0.001) were prognostic factors for a 3-year disease-free survival. ECOG performance status (p=0.039, HR=3.95; 95% CI=1.07-14.56), weight loss (p=0.024, HR=5.98; 95% CI=1.27-28.11), and hemoglobin level (p=0.038, HR=3.83; 95% CI=1.07-13.67) were independent prognostic factors for a 3-year disease-free survival.

Table 1. Demographic data of the patients.

	Number of patients (%)
Gender	
Male	176 (84)
Female	34 (16)
Age	
<65 yrs	146 (70)
≥65 yrs	64 (30)
Smoking	142 (68)
Alcohol intake	37 (18)
Comorbidity	74 (35)
Performance status	
ECOG0-1	115 (55)
>ECOG1	95 (45)
Location	
Oral cavity-oropharynx	46 (22)
Paranasal sinus	12 (6)
Nasopharynx	42 (20)
Larynx -hypopharynx	92 (44)
Salivary gland	13 (6)
Unknown primary focus	5 (2)
Histopathology	
Squamous cell carcinoma	184 (88)
Other	26 (12)
Perineural invasion	29/70 (41)
Lymphovascular invasion	24/68 (35)
Grade	
Grade1	48/172 (28)
Grade 2	64/172 (37)
Grade 3	60/172 (35)
Surgical margin	
Negative	69/90 (77)
Close or pozitive	21/90 (23)
Stage	
Stage I	33 (16)
Stage II	44 (21)
Stage III	51 (24)
Stage IVA,B	76 (36)
Stage IVC	6 (3)
Treatment	
Surgery	26 (12)
Radiotherapy	42 (20)
Chemoradiotherapy	55 (26)
Surgery+RT*/CRT†	75 (36)
Palliative treatment	12 (6)

*RT: Radiotherapy, †CRT: Chemoradiotherapy

In a univariate analysis, 3-year local disease control, overall and disease-free survival rates, and prognostic factors effecting survival rates are shown in Table 2, and independent prognostic factors in multivariate analysis are presented in Table 3.

Discussion

In head and neck cancers, deformation of anatomic structure exposes the patient to serious psychologic, and functional problems. Weight loss developed as a result of nutritional problems secondary to the adverse effects of the disease, and treatments, decreases in hemoglobin levels, and related deterioration in the performance status can further worsen prognosis of the patients with head, and

Table 2. Prognostic factors effective on local control, and survival rates of the patients in univariate analysis.

	N	3-year LC	P values	3-year OS	p values	3-year DFS	p values
Gender							
Male	176	72	0.397	53	0.587	53	0.587
Female	34	66		51		51	
Age							
<65 yrs	146	71	0.236	62	0.371	55	0.536
≥65 yrs	64	75		51		48	
Comorbidity							
Absent	137	73	0.537	65	0.028	58	0.045
Presence	73	71		48		43	
Performance status							
ECOG0-1	115	79	0.006	79	<0.001	73	<0.001
>ECOG1	95	60		39		31	
Hemoglobin							
≥12 mg/dL	129	74	0.189	68	<0.001	63	<0.001
<12 mg/dL	48	61		38		36	
Weight loss							
Absent	108	83	0.002	76	<0.001	68	<0.001
Present	102	58		46		39	
Location							
Oral cavity-oropharynx	44	56	0.003	40	0.007	40	0.007
Paranasal sinus	12	36		25		25	
Nasopharynx	42	84		58		58	
Larynx-hipopharynx	92	79		57		57	
Salivary gland	13	74		75		75	
Stage							
Stage I	33	92	<0.001	77	<0.001	77	<0.001
Stage II	44	75		72		72	
Stage III	51	81		60		60	
Stage IV	76	53		33		31	
Grade							
Grade 1	47	64	0.390	50	0.422	50	0.422
Grade 2	63	76		59		59	
Grade 3	60	68		44		44	
Perineural invasion							
Absent	41	80	0.011	68	0.017	68	0.017
Present	29	45		51		51	
Lymphovascular invasion							
Absent	44	68	0.973	69	0.022	69	0.022
Present	24	67		50		50	
Surgical margin							
Negative	68	73	0.053	63	0.422	63	0.868
Close or positive	21	48		60		60	
Interruption of RT							
No	142	71	0.418	63	0.041	57	0.088
Yes	35	62		46		45	
Mucositis							
Absent	39	76	0.098	74	0.136	65	0.075
Present	142	66		57		50	

LC: local control, OS: overall survival, DFS: disease-free survival

neck cancers. However closer monitorization of treatment-related adverse effects, alleviating nutritional problems, and amelioration of hematological parametres can ensure improvement in prognosis. In this study, disease-specific prognostic factors as stage, and location of the disease, and perineural invasion as well as weight loss, hemoglobin levels, postponement of RT, performance status, local disease control have been detected to be associated with overall and disease-free survival rates.

Comorbidity is defined as a disease or a disorder such as hypertension, heart disease, and diabetes mellitus etc. which accompanies primary malignancy of the patient. Since comorbidities affect treatment decision-making process, course of the treatment, and quality of life of the patients, they are considered as prognostic factors. Zhang et al. indicated comorbidities as independent prognostic factors in 205 laryngeal cancer patients who had undergone surgical interventions.[4] Chen et al. demonstrated comorbidity as an independent prognostic factor in 182 advanced stage laryngeal cancer patients.[5] Similarly Montero et al. also reported comorbidity as an independent prognostic factor for survival in 114 patients with locally advanced stage hypopharyngeal, and laryngeal cancers under combination therapy.[6] In the present study, similar to these two studies, presence of a comorbidity affected prognosis but it did not face us as an independent prognostic factor. Presence of a comorbidity has become an important factor in 3-year overall, and disease-free survival rates. However, a marked impact on local disease control was not observed.

Performance status of the patients is an important parameter in both decision-making process for treatment, and course of the treatment. Besides its prognostic significance for many cancer types has been demonstrated. Taylor et al. (1994) indicated that performance status effected progression-free survival rates among 215 patients with locally advanced head and neck cancer who had undergone induction chemotherapy followed by CRT.[7] Jones et al. investigated 2701 patients with head and neck surgery, and demonstrated the presence of a correlation between performance status, and survival rates.[8] Chang et al. indicated that among head and neck cancer patients who had undergone concurrent CRT , those with worse ECOG performance status had a risk of premature death, and so they were not eligible candidates for CRT.[9] Rades et al. reported that among 170 advanced stage head and neck cancer patients, 3-year local disease control, and overall survival rates were affected more adversely in those with an ECOG performance status relative to patients with a lower ECOG grade.[10] In this study, ECOG performance status was determined as an independent prognostic factor for 3-year overall, and disease-free survival rates. It has also become a determinative factor for local disease control.

The patients with relatively lower hemoglobin levels had tumors less responsive to treatment when compared to those with normal hemoglobin levels. The correlation between hemoglobin levels and tumoral response was demonstrated (in 23/25 studies) in a meta-analysis published in 1991. In this meta-analysis, lower hemoglobin values were seen to be an important predictive factor which had an unfavorable impact on the treatment of head, and neck, cervix, lung, and bladder cancers.[11] Rutkowski et al. investigated the significance of variations in hemoglobin values in 78 T2 supraglottic cancers, and reported that lower baseline hemoglobin concentrations at the start of RT, affected overall survival rates unfavorably.[12] Van Acht et al. stated that in patients with supraglottic laryngeal cancers lower hemoglobin levels at the end of the treatment were indicative of poor disease-free survival.[13] Tarnawski et al. determined that lower hemoglobin levels both at the start, and end of the treatment of supraglottic laryngeal cancers are an independent prognostic factor in the local control of the disease.[14] McCloskey et al. reported that relatively lower pretreatment hemoglobin level (<12 g/dL) in 78 head and neck cancer patients under definitive CRT is an independent prognostic factor for local disease control.[15] In our study hemoglobin levels below 12 g/dL effected 3-year overall, and disease-free survival rates without any impact on local disease control rates. At the same time, lower hemoglobin values had an independent prognostic effect on overall and disease-free survival. Regular monitorization of hemoglobin levels during therapy, and supportive therapy can eliminate this unfavorable effect.

Table 3. Independent prognostic factors effective on local control, and survival rates of the patients in multivariate analysis.

	HR 95%	Confidence interval (CI)	P values
3-year local control			
Weight loss	0.034	3.01	1.08-8.36
Perineural invasion (+)	0.052	2.57	0.99-6.68
3-year overall survival rates			
>ECOG1	0.040	3.52	1.06-11.70
Weight loss	0.025	6.21	1.26-30.54
Hemoglobin <12 g/dL	0.012	5.59	1.46-21.42
Interruption of RT	0.006	4.73	1.55-14.40
3-year-disease-free survival rates			
>ECOG1	0.039	3.95	1.07-14.56
Weight loss	0.024	5.98	1.27-28.11
Hemoglobin <12 g/dL	0.038	3.83	1.07-13.67

HR: hazard ratio, RT: radiotherapy

In patients with head and neck cancers, weight loss before, during, and after treatment can develop generally because of tumor-related physical abnormalities (obstructions inducing dysphagia), patient-related causes (chronic inflammation, and formation of cytokines) and adverse effects of treatments applied.[16-18] Location of the tumor also constitutes a risk factor for weight loss. In 50% the patients with head and neck surgery, weight loss was detected at the time of diagnosis, while it can develop as a consequence of treatment-related side effects.[19] Nausea and vomiting developed secondary to RT in patients with head and neck cancers are responsible for 30% of cases with weight loss.[20] Nourissat et al. investigated 540 patients with head, and neck cancers, and determined weight loss of 5% relative to baseline was the predictive critical weight loss occurred during RT.[21] The same researchers demonstrated that oral mucositis, pretreatment odinophagia, and dysphagia, location of the tumor (oral cavity, oropharynx, hypopharyns, and suproglottic laryunx carcinoma), stage of the disease (Stage II), and eating low-energy dense foods are independent prognostic factors for weight loss.[22] Several investigators have pointed out to the relationship between weight loss, and survival rates in cases with head and neck cancers.[23-25] In our study, loss of 5% of body weight relative to baseline was evaluated as weight loss. As outcomes of both the disease, and treatments applied nearly half of the patients lost weight despite use of oral nutritional supplements in 56% of the patients undergoing RT. Weight loss had an impact on local control, overall, and disease-free survival, and it had become an independent prognostic risk factor for 3-year overall, and disease-free survival, and local disease control.

In head, and neck cancers, deferral of RT is associated with lower survival, and local disease control rates because of accelerated repopulation of cancer stem cells.[26-28] Local disease control rates change dependent on the delay in the application of RT. Various studies have indicated that interruption of RT for one day, and one week decreases local disease control rates for 1.4%, and 2-25%, respectively.[29-31] Fesinmeyer et al. investigated 3864 patients aged ≥66 years with head and neck cancers between the years 1997 and 2003, and demonstrated statistically significant difference in median survival rates in patients with laryngeal, and salivary gland cancers whose RT was delayed for 5 days or longer. Median survival times in larynx cancer patients with or without postponed RT, were 66.9 and 37.3 months ($p<0.001$), respectively. Corresponding values for patients with salivary gland cancers were detected as 57.8, and 38.5 months, respectively ($p=0.006$). Besides, authors reported that risk of mortality was 68% higher in larynx cancer patients whose RT was deferred relative to those without any interruption.[32] McCloskey et al. demonstrated that one week deferral of RT in 78 patients with head and neck cancers was an independent prognostic factor for local control.[15] However, in the present study postponement of RT for 5 days or longer was an independent prognostic factor for 3-year overall survival. This factor was not effective on local control, and disease-free survival.

Mucositis is a side effect of RT, however it is observed in increasing frequency in association with CRT. During therapy, it impairs nutritional status, and quality of life of the patients with resultant interruption of their treatments, and weight loss. Its impact on these two prognostic parameters suggest that oral mucositis can indirectly, and unfavorably effect survival, and local control of the disease. However Wolff et al. investigated 216 patients with locally advanced stage head and neck carcinoma who had undergone CRT, and demonstrated a positive correlation between higher grade acute organ toxicity (mucositis, dysphagia, and skin reaction), local disease control, and survival rates.[33] In the present study, among patients who had received RT or CRT, grade 1-2 , and 3-4 oral mucositis developed in 51% and 28% of the cases and 59% them complained of nausea, and vomiting as adverse effects of the therapy. Presence of mucositis was not found to be statistically significant as for 3-year overall survival, disease-free survival, and local disease control rates.

Conclusion

Weight loss, lower hemoglobin levels, interruption of RT, and performance status of the patients affected overall survival rates adversely. While local disease control was affected unfavourably by weight loss, the lower hemoglobin level, weight loss and performance status of the patients had a negative impact on disease-free survival rates.

Conflict of Interest: No conflicts declared.

References

1. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. Cancer statistics, 2009. CA Cancer J Clin 2009;59:225-49.
2. Haydaroğlu A, Bölükbaşı Y, Özsaran Z. Ege Üniversitesi'nde kanser kayıt analizleri: 34134 Olgunun değerlendirmesi. Türk Onkoloji Dergisi 2007;22:22-8.
3. Bourhis J, Overgaard J, Audry H, et al.; Meta-Analysis of Radiotherapy in Carcinomas of Head and neck (MARCH) Collaborative Group. Hyperfractionated or accelerated radiotherapy in head and neck cancer: a meta-analysis. Lancet 2006;368: 843-54.
4. Zhang SY, Lu ZM, Luo XN, et al. Retrospective analysis of prognostic factors in 205 patients with laryngeal squamous cell carcinoma who underwent surgical treatment. PLoS One 2013;8:e60157.

5. Chen AY, Matson LK, Roberts D, Goepfert H. The significance of comorbidity in advanced laryngeal cancer. Head Neck 2001;23: 566-72.
6. Montero EH, Trufero JM, Romeo JA, Terré FC. Comorbidity and prognosis in advanced hypopharyngeal-laryngeal cancer under combined therapy. Tumori 2008;94:24-9.
7. Taylor SG 4th, Murthy AK, Vannetzel JM, et al. Randomized comparison of neoadjuvant cisplatin and fluorouracil infusion followed by radiation versus concomitant treatment in advanced head and neck cancer. J Clin Oncol 1994;12:385-95.
8. Jones AS, Fenton JE, Husband DJ. Performance data and survival in head and neck cancer. Clin Otolaryngol Allied Sci 2000;25:396-403.
9. Chang PH, Yeh KY, Huang JS, et al. Pretreatment performance status and nutrition are associated with early mortality of locally advanced head and neck cancer patients undergoing concurrent chemoradiation. Eur Arch Otorhinolaryngol 2013;270:1909-15.
10. Rades D, Seibold ND, Gebhard MP, Noack F, Schild SE, Thorns C. Prognostic factors (including HPV status) for irradiation of locally advanced squamous cell carcinoma of the head and neck (SCCHN). Strahlenther Onkol 2011;187:626-32.
11. Dische S. Radiotherapy and anemia – the clinical experience. Radiother Oncol 1991;20:35-40.
12. Rutkowski T, Wygoda A, Skladowski K, et al. Predictors of radiotherapy outcome in patients with T2 supraglottic carcinoma. Eur Arch Otorhinolaryngol 2012;269:923-9.
13. van Acht MJ, Hermans J, Boks DE, Leer JW. The prognostic value of hemoglobin and a decrease in hemoglobin during radiotherapy in laryngeal carcinoma. Radiother Oncol 1992;23:229-35.
14. Tarnawski R, Skladowski K, Maciejewski B. Prognostic value of hemoglobin concentration in radiotherapy for cancer of supraglottic larynx. Int J Radiat Oncol Biol Phys 1997;38:1007-11.
15. McCloskey SA, Jaggernauth W, Rigual NR, et al. Radiation treatment interruptions greater than one week and low hemoglobin levels (12 g/dL) are predictors of local regional failure after definitive concurrent chemotherapy and intensity-modulated radiation therapy for squamous cell carcinoma of the head and neck. Am J Clin Oncol 2009;32:587-91.
16. Jager-Wittenaar H, Dijkstra PU, Vissink A, et al. Critical weight loss in head and neck cancer – prevalence and risk factors at diagnosis: an explorative study. Support Care Cancer 2007;15:1045-50.
17. Beaver ME, Matheny KE, Roberts DB, Myers JN. Predictors of weight loss during radiation therapy. Otolaryngol Head Neck Surg 2001;125:645-8.
18. Mangar S, Slevin N, Mais K, Sykes A. Evaluating predictive factors for determining enteral nutrition in patients receiving radical radiotherapy for head and neck cancer: a retrospective review. Radiother Oncol 2006;78:152-8.
19. Lees J. Incidence of weight loss in head and neck cancer patients on commencing radiotherapy treatment at a regional oncology centre. Eur J Cancer Care (Engl) 1999;8:133-6.
20. Feyer PC, Maranzano E, Molassiotis A, Roila F, Clark-Snow RA, Jordan K; MASCC/ESMO. Radiotherapy-induced nausea and vomiting (RINV): MASCC/ESMO guideline for antiemetics in radiotherapy: update 2009. Support Care Cancer 2011;19 Suppl 1: S5-14.
21. Nourissat A, Bairati I, Samson E, et al. Predictors of weight loss during radiotherapy in patients with stage I or II head and neck cancer. Cancer 2010;116:2275-83.
22. Nourissat A, Bairati I, Fortin A, et al. Factors associated with weight loss during radiotherapy in patients with stage I or II head and neck cancer. Support Care Cancer 2012;20:591-9.
23. van Bokhorst-de van der Schuer, van Leeuwen PA, Kuik DJ, et al. The impact of nutritional status on the prognoses of patients with advanced head and neck cancer. Cancer 1999;86:519-27.
24. Regueiro CA, Aragón G, Millán I, Valcárcel FJ, de la Torre A, Magallón R. Prognostic factors for local control, regional control and survival in oropharyngeal squamous cell carcinoma. Eur J Cancer 1994;30A:2060-7.
25. Hammerlid E, Wirblad B, Sandin C, et al. Malnutrition and food intake in relation to quality of life in head and neck cancer patients. Head Neck 1998;20:540-8.
26. Russo G, Haddad R, Posner M, Machtay M. Radiation treatment breaks and ulcerative mucositis in head and neck cancer. Oncologist 2008;13:886-98.
27. Bese NS, Hendry J, Jeremic B. Effects of prolongation of overall treatment time due to unplanned interruptions during radiotherapy of different tumor sites and practical methods for compensation. Int J Radiat Oncol Biol Phys 2007;68:654-61.
28. Tarnawski R, Fowler J, Skladowski K, et al. How fast is repopulation of tumor cells during the treatment gap? Int J Radiat Oncol Biol Phys 2002;54:229-36.
29. Barton MB, Keane TJ, Gadalla T, Maki E. The effect of treatment time and treatment interruption on tumour control following radical radiotherapy of laryngeal cancer. Radiother Oncol 1992;23: 137-43.
30. Fowler JF, Lindstrom MJ. Loss of local control with prolongation in radiotherapy. Int J Radiat Oncol Biol Phys 1992;23:457-67.
31. Lindstrom MJ, Fowler JF. Re-analysis of the time factor in local control by radiotherapy of T3T4 squamous cell carcinoma of the larynx. Int J Radiat Oncol Biol Phys 1991;21:813-7.
32. Fesinmeyer MD, Mehta V, Blough D, Tock L, Ramsey SD. Effect of radiotherapy interruptions on survival in medicare enrollees with local and regional head-and-neck cancer. Int J Radiat Oncol Biol Phys 2010;78:675-81.
33. Wolff HA, Bosch J, Jung K, et al. High-grade acute organ toxicity as positive prognostic factor in primary radio(chemo)therapy for locally advanced, inoperable head and neck cancer. Strahlenther Onkol 2010;186:262-8.

Please cite this article as: Yücel B, Eren MF, Akkaş Atesever E, Kaçan T, Hasbek Z, Şeker MM. Prognosis in head and neck cancer: the importance of the patient-, and treatment-related factors. J Med Updates 2013;3(3):109-115.