

# A New Survival Score for Patients Scheduled for Palliative Irradiation of Locally Advanced Carcinoma of the Head-and-Neck

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**Abstract.** *Background/Aim:* Patients with advanced squamous cell carcinoma of the head-and-neck (SCCHN) may be assigned to palliative irradiation. A survival score was developed for this group to support treatment personalization. *Patients and Methods:* Seventy-eight patients who received palliative irradiation for SCCHN and had complete data regarding performance score, pre-radiotherapy hemoglobin levels, and main tumor site were included in this retrospective study. Six-month survival rates of these factors were divided by 10 (factor scores) and added for each patient (total patient scores). *Results:* Total patient scores ranged between 8 and 15 points. Three groups were designed based on the 6-month survival rates, namely 8-9 (n=15), 11-13 (n=36), and 14-15 (n=27) points. Six-month survival rates were 13%, 28%, and 63%, and median survival times were 1, 2, and 11 months (p=0.001). *Conclusion:* A new survival score including three prognostic groups was developed. This new tool can help physicians when designing personalized treatments for patients with SCCHN scheduled for palliative irradiation.

The majority of patients with squamous cell carcinoma of the head-and-neck (SCCHN) are candidates for a curative treatment approach including surgery and/or radio-(chemo)therapy (1, 2). However, a considerable number of patients are not suitable for

such a treatment and are scheduled for palliative irradiation. This applies particularly to patients with metastatic disease, locally or loco-regionally very advanced tumors and to patients with significant co-morbidity, a poor performance status or old age (3, 4). For palliative irradiation, different dose-fractionation schedules are available including ultra-short regimens such as quad shot (14 Gy in 4 fractions over only 2 days), short-course regimens such as 20-24 Gy with daily fractions of 4.0 Gy given five times per week, intermediate-course regimens such as 36-39 Gy with daily fractions of 3.0 Gy, and long-course regimens such as 50-60 Gy with daily fractions of 2.0-2.5 Gy (1, 4, 5). The patient's survival prognosis should be considered when selecting a palliative dose-fractionation regimen for loco-regionally advanced SCCHN. If the prognosis is poor, the patient should not receive a time-consuming regimen but one which is able to relieve existing symptoms and does not take longer than necessary. Patients with longer expected survival can benefit from longer-course regimens in terms of longer disease control and lower probability of late toxicities. Therefore, survival scores are important because they allow estimating the patient's prognosis prior to radiation therapy. Such scores exist for irradiation of metastatic SCCHN (6, 7). The current study was performed to add a new survival score for patients with SCCHN scheduled for palliative local or loco-regional irradiation.

## Patients and Methods

Seventy-eight patients who were treated with palliative irradiation for advanced SCCHN between 2000 and 2020 and had complete data regarding Eastern Cooperative Oncology Group performance score (ECOG-PS), hemoglobin levels prior to radiotherapy, and primary tumor site were included in this retrospective study. These patients were previously analyzed in a study that investigated ten

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pre-radiotherapy factors (age, gender, ECOG-PS, pre-radiotherapy hemoglobin level, primary tumor site and stage, nodal stage, distant metastasis, histologic grade, p16-status) and four treatment-related factors (radiation dose, completion of radiation therapy, upfront surgery, systemic treatment) for associations with survival (8). Of the ten pre-radiotherapy factors, pre-radiotherapy hemoglobin levels of  $\geq 12$  g/dl (vs.  $< 12$  g/dl) showed significant associations with better survival in both univariate and multivariate analyses. Moreover, trends toward better survival were found on univariate analyses for ECOG-PS 0-2 (vs. 3) and favorable tumor site (oropharynx, larynx or oral cavity/floor of mouth vs. hypopharynx). These three factors (Table I) were included in the survival score developed in the present study approved by the local Ethics Committee (University of Lübeck, 18-130A). In seven patients, additional data regarding pre-radiotherapy hemoglobin levels were collected.

*Statistical analyses.* The 6-month survival rates of the three factors, pre-radiotherapy hemoglobin level, ECOG-PS, and tumor site were divided by 10 to receive the factor scores (Table II). For each patient, the three factor scores were added to obtain the total patient score. Based on the total patient scores, prognostic groups were designed and compared for survival using the Kaplan–Meier method and the log-rank test. A *p*-value of  $< 0.05$  was regarded as indicating statistical significance. The software used for the statistical analyses was JMP Pro 14.1.0 (SAS Institute Inc., Cary, NC, USA).

**Results**

The total patient scores ranged between 8 and 15 points. No patient had 10 points. The corresponding 6-month survival rates were 0% (0/3) for 8 points, 17% (2/12) for 9 points, 25% (4/16) for 11 points, 29% (5/17) for 12 points, 33% (81/3) for 13 points, 50% (5/10) for 14 points and 79% (12/17) for 15 points, respectively (Figure 1).

Three prognostic groups were designed based on these 6-month survival rates, namely 8-9 points (n=15), 11-13 points (n=36), and 14-15 points (n=27). The corresponding 6-month survival rates were 13%, 28%, and 63%, respectively, and the 12-month survival rates were 0%, 15%, and 37%, respectively (Figure 2, *p*=0.001). The median survival times were 1 month, 2 months, and 11 months, respectively.

**Discussion**

The concept of treatment personalization is important to achieve optimal individual outcomes for patients with advanced-stage SCCHN who are scheduled for palliative irradiation. Personalized treatment regimens should be based on several factors including the patient’s survival prognosis. Therefore, it is desirable to be able to estimate an individual patient’s remaining lifespan as precisely as possible before initiation of treatment. Such an estimation can be considerably facilitated with the availability of prognostic factors or, even better, prognostic scores. Survival scores for palliative irradiation of patients with SCCHN are already available for those with metastatic disease. In 2015, a survival score was

Table I. Distribution of the tree factors used for the survival score.

Factor	N patients (%)
Eastern Cooperative Oncology	
Group performance score	
0-2	61 (78)
3	17 (22)
Pre-radiotherapy hemoglobin level	
$< 12$ g/dl	45 (58)
$\geq 12$ g/dl	33 (42)
Main tumor site	
Oropharynx	42 (54)
Hypopharynx	18 (23)
Larynx	8 (10)
Oral cavity/Floor of mouth	10 (13)

Table II. Six-month survival rates of the three prognostic factors (8) and the corresponding factor scores.

Factor	6-months survival rate (%)	Factor score
Eastern Cooperative Oncology		
Group performance score		
0-2	43	4
3	32	3
Pre-radiotherapy hemoglobin level		
$< 12$ g/dl	26	3
$\geq 12$ g/dl	57	6
Main tumor site		
Oropharynx	48	5
Hypopharynx	23	2
Larynx	44	4
Oral cavity/Floor of mouth	42	4

developed for patients with brain metastases from SCCHN (6). This tool included three prognostic groups with 6-month survival rates of 0%, 50%, and 100%, respectively. In the same year, a survival score for patients with SCCHN and patients with metastatic spinal cord compression was reported (7). This score included four groups with 6-month survival rates of 0%, 27%, 71%, and 100%, respectively.

The present study was conducted to provide an additional survival score for patients with advanced SCCHN receiving local or loco-regional irradiation with palliative intent. The methodology used in this study was similar to the methodology of the two scores for metastatic SCCHN (6, 7). The new score developed in the current study is based on prognostic factors significantly associated with survival or at least showing a trend. It consists of three groups with significantly different 6-month survival rates.

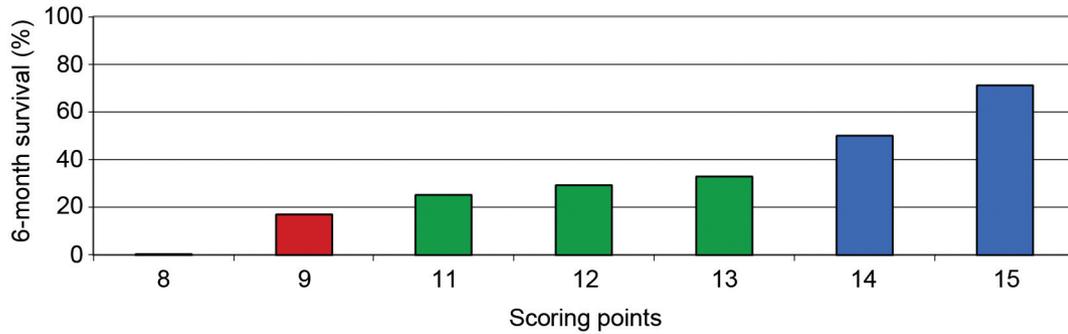


Figure 1. Six-month survival rates of the total patient scores that ranged between 8 and 15 points.

Patients achieving 8-9 points had the poorest survival prognoses with a 6-month survival rate of only 13% and a median survival time of only 1 month. These patients may be considered candidates for an ultra-short regimen such as quad shot or for best supportive care alone. Patients who achieved 11-13 points had better but still poor survival prognoses. The median survival time was only 2 months, and the 6-month survival rate was 28%. These patients appear good candidates for a short-course regimen with a total dose of 20-24 Gy (5×4.0 Gy per week) or an intermediate-course regimen with a dose of 36-39 Gy (5×3.0 Gy per week). Patients achieving 14-15 points had the most favorable survival prognoses with a 6-month survival rate of 63% and a median survival time of 11 months. For these patients, loco-regional control of their disease for a longer time is more important. Moreover, the majority of these patients will live long enough to experience late radiation-related toxicities. The risk of experiencing such toxicities increases with time. However, when applying this new score, one should be aware that it has been developed from retrospective data. Thus, a risk of a hidden selection bias exists. Moreover, two of the factors included in the scoring system were not significant but showed only a trend in the preceding study (8).

In summary, a new survival score including three prognostic groups with significantly different survival rates and median survival times was developed. This new tool can help physicians who wish to assign a personalized treatment to a patient with SCCHN scheduled for palliative irradiation.

### Conflicts of Interest

The Authors report no conflicts of interest related to the present study.

### Authors' Contributions

All Authors participated in the design of the study. C.S. collected the data that were analyzed by S.E.S. and D.R. The article drafted by D.R. and S.E.S. was reviewed and finally approved by all Authors.

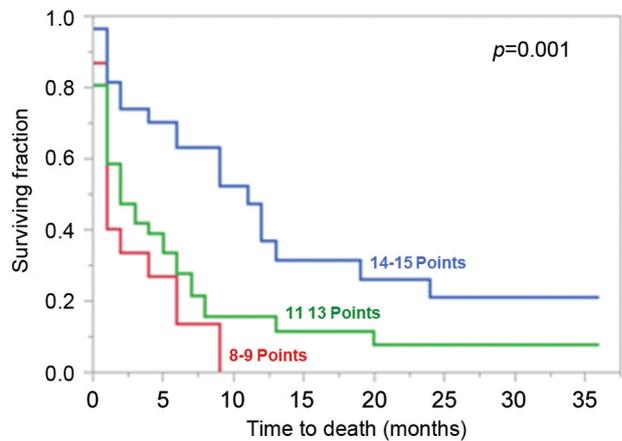


Figure 2. Kaplan-Meier curves for survival of the three prognostic groups: 8-9 points, 11-13 points, and 14-15 points. The *p*-value was calculated using the log-rank test.

### References

- 1 Chow LQM: Head and neck cancer. *N Engl J Med* 382(1): 60-72, 2020. PMID: 31893516. DOI: 10.1056/NEJMra1715715
- 2 Pignon JP, le Maître A, Maillard E, Bourhis J and MACH-NC Collaborative Group: Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): an update on 93 randomised trials and 17,346 patients. *Radiother Oncol* 92(1): 4-14, 2009. PMID: 19446902. DOI: 10.1016/j.radonc.2009.04.014
- 3 Grewal AS, Jones J and Lin A: Palliative radiation therapy for head and neck cancers. *Int J Radiat Oncol Biol Phys* 105(2): 254-266, 2019. PMID: 31128145. DOI: 10.1016/j.ijrobp.2019.05.024
- 4 Shahid Iqbal M, Kelly C, Kovarik J, Goranov B, Shaikh G, Morgan D, Dobrowsky W and Paleri V: Palliative radiotherapy for locally advanced non-metastatic head and neck cancer: A systematic review. *Radiother Oncol* 126(3): 558-567, 2018. PMID: 29370986. DOI: 10.1016/j.radonc.2017.12.011
- 5 Corry J, Peters LJ, Costa ID, Milner AD, Fawns H, Rischin D and Porceddu S: The 'QUAD SHOT' – a phase II study of

- palliative radiotherapy for incurable head and neck cancer. *Radiother Oncol* 77(2): 137-142, 2005. PMID: 16260054. DOI: 10.1016/j.radonc.2005.10.008
- 6 Rades D, Dziggel L, Hakim SG, Rudat V, Janssen S, Trang NT, Khoa MT and Bartscht T: Predicting survival after irradiation for brain metastases from head and neck cancer. *In Vivo* 29(5): 525-528, 2015. PMID: 26359409.
- 7 Rades D, Schild SE, Karstens JH and Hakim SG: Predicting survival of patients with metastatic epidural spinal cord compression from cancer of the head-and-neck. *Anticancer Res* 35(1): 385-388, 2015. PMID: 25550576.
- 8 Staackmann C, Ribbat-Idel J, Perner S, Idel C, Bruchhage KL, Hakim SG, Schild SE and Rades D: Palliative local radiotherapy for advanced squamous cell carcinoma of the head-and-neck: Prognostic factors of survival. *Anticancer Res* 41(6), in press, 2021.

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