

Survival Following Palliative Radiotherapy for Head and Neck Squamous Cell Carcinoma: Examining Treatment Indications in Elderly Patients

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Abstract. *Background/Aim:* This study investigated the survival outcomes of patients with head and neck squamous cell carcinoma (HNSCC) undergoing palliative radiotherapy, particularly focusing on challenges and factors associated with older age, providing insights into appropriate palliative radiotherapy use in this demographic. *Patients and Methods:* A retrospective study was conducted using electronic medical records of 73 patients with HNSCC who were deemed unsuitable for curative therapy. Palliative radiotherapy involved a uniform dose of 30 Gy in 10 fractions. Survival analysis was performed using Kaplan–Meier method, and multivariate analysis identified significant prognostic factors. *Results:* The median overall survival was 7.5 months, with no significant difference between age groups. Karnofsky performance status (KPS) >70 correlated with favorable survival. Multivariate analysis confirmed KPS as an independent prognostic factor (hazard ratio=1.949, $p=0.031$). *Conclusion:* The results of this study align with those of previous studies, emphasizing the importance of palliative radiotherapy for HNSCC treatment. Optimal dose fractionation regimens remain undetermined, and tailored

approaches that consider factors, such as age and performance status are crucial. Individualized, comprehensive assessments and supportive care measures enhance patient well-being, reflecting palliative care principles.

Head and neck squamous cell carcinoma (HNSCC) poses a significant global health challenge, with varying incidence rates in different regions (1). This cancer type is often linked to exposure to tobacco-derived carcinogens, excessive alcohol consumption, or viral infections (2). Notably, many patients are diagnosed with advanced-stage HNSCC despite lacking prior clinical signs of premalignancy (3).

Concurrent chemoradiotherapy is the standard treatment for locally advanced HNSCC (4). The established regimen involves administering radiotherapy at a dose of 70 Gy over 35 fractions concurrently with triweekly cisplatin, based on the protocol derived from the RTOG 91-11 trial (5). However, this approach has drawbacks, most notably a high incidence of grade 3-4 mucositis affecting 43% of patients. Japan is witnessing a rapid increase in aging population, leading to a higher prevalence of cancer among older adults (6). Older patients with HNSCC present unique challenges, including comorbidities, reduced functional status, and limited tolerance for aggressive treatments, such as concurrent chemoradiotherapy (7, 8). Palliative radiotherapy has emerged as a crucial therapeutic option for managing advanced HNSCC, particularly when curative interventions may not be feasible or suitable (9, 10). Palliative radiotherapy also offers a rationale for tumor shrinkage, hemostasis, and pain relief (11, 12).

Accordingly, in this study, we aimed to investigate the survival outcomes of patients with HNSCC undergoing palliative radiotherapy, considering specific challenges and factors associated with older age, and offer valuable insights into the appropriate use of palliative radiotherapy in these patients. Ultimately, the results will contribute to making

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better-informed and personalized treatment decisions for this demographic, thereby improving their overall quality of life and outcomes.

Patients and Methods

This retrospective study utilized electronic medical records of the involved institution. All patients were pathologically diagnosed with squamous cell carcinoma and were deemed unsuitable for curative therapy, such as radical surgery or chemoradiotherapy, for HNSCC. Their treatment was initiated between March 2013 and April 2023. For palliative radiotherapy, the fractionation regimens were administered with a uniform dose of 30 Gy in 10 fractions, without administering concurrent systemic anticancer therapy.

Details of radiotherapy and date of death were obtained from the medical records. All patients received three-dimensional radiotherapy using 6-10 MV X-ray external beams, without utilizing intensity-modulated radiotherapy. Planning computed tomography (CT) scans were obtained using a thermoplastic mask on a flat board, with a 5 mm slice thickness. Clinical target volume (CTV) encompassed the primary tumor and the involved lymph node, whereas planning target volume (PTV) included the CTV with a 3-5 mm margin. Prophylactic lymph node irradiation was not employed. A total dose of 30 Gy in 10 fractions was prescribed to the isocenter.

All statistical analyses were conducted using R software. Survival time was measured from the first day of radiotherapy. Actuarial survival curves were constructed using the Kaplan–Meier method and compared using the log-rank test. The multivariate analysis was performed to identify variables significant for survival. A *p*-value of <0.05 was considered significant.

Results

In this study, the study cohort included 73 participants (male, *n*=64; female, *n*=9). The median age at the start of palliative radiotherapy was 73 years (range=46-98 years) (Table I). The patients exhibited varying Karnofsky performance statuses (KPS), with 9 patients at 90, 31 at 80, 22 at 70, 5 at 60, 5 at 50, and 1 at 40. The primary tumor sites were the hypopharynx in 22 patients, oral cavity in 20, oropharynx in 16, nasopharynx in 6, larynx in 5, and other locations in 4, including 2 in the paranasal sinus, and 1 each in the salivary gland and external ear canal. Notably, 26 cases were already metastatic at the initiation of radiotherapy.

After a median follow-up duration of 5.5 months (range=0.2-81.9 months), the median overall survival (OS) period was 7.5 months, with a 95% confidence interval (CI) of 5.5-12.0%. The 1-year OS rate was 35.6% (95%CI=22.8-48.5%). No statistically significant difference in OS was observed between age groups, with a median OS period of 8.4 months for patients aged ≤70 years and 7.4 months for those aged >70 years (*p*=0.733) (Figure 1). Moreover, no significant variations in OS were observed in terms of sex (*p*=0.585) or the presence of distant metastasis (*p*=0.720), and patients with KPS scores exceeding 70 exhibited significantly favorable survival rates (*p*=0.0476).

Table I. Profile of patients undergoing palliative radiotherapy for head and neck squamous cell carcinoma at our medical facility.

Variables	Number	Percentage
Age, years, median [range]	73 [46-98]	
Sex		
Male	64	88%
Female	9	12%
Karnofsky performance status		
90	9	12%
80	31	42%
70	22	30%
60	5	7%
50	5	7%
40	1	1%
Primary site		
Hypopharynx	22	30%
Oral cavity	20	27%
Oropharynx	16	22%
Nasopharynx	6	8%
Larynx	5	7%
Others	4	5%
Clinical stage		
II	4	5%
III	6	8%
IVA	15	21%
IVB	13	18%
IVC	22	30%
Recurrence	13	18%
Distant metastasis		
Absent	47	64%
Present	26	36%

In the multivariate analysis, KPS remained as an independent prognostic factor for survival, with a hazard ratio of 1.949 (95%CI=1.062-3.578, *p*=0.031) (Table II).

Discussion

The results of this retrospective analysis of survival following palliative radiotherapy for HNSCC are consistent with those of previous studies. Viani *et al.* conducted a meta-analysis of palliative radiotherapy outcomes in patients with incurable head and neck cancer and reported a median OS period of 6.5 months for 1,986 patients (13). Desideri *et al.* analyzed 33 studies focusing on palliative radiotherapy for advanced HNSCC in older patients and reported a median OS period of 7.7 months (14).

To our knowledge, an optimal dose fractionation regimen has not been established for palliative radiotherapy in head and neck cancer. Srivastava *et al.* reported favorable outcomes with the Christie regimen in Northern England, which consists of a total dose of 50 Gy delivered over 16 fractions over 3.2 weeks, (15). The RTOG 8502 regimen, also called QUAD SHOT, involves consecutive daily doses

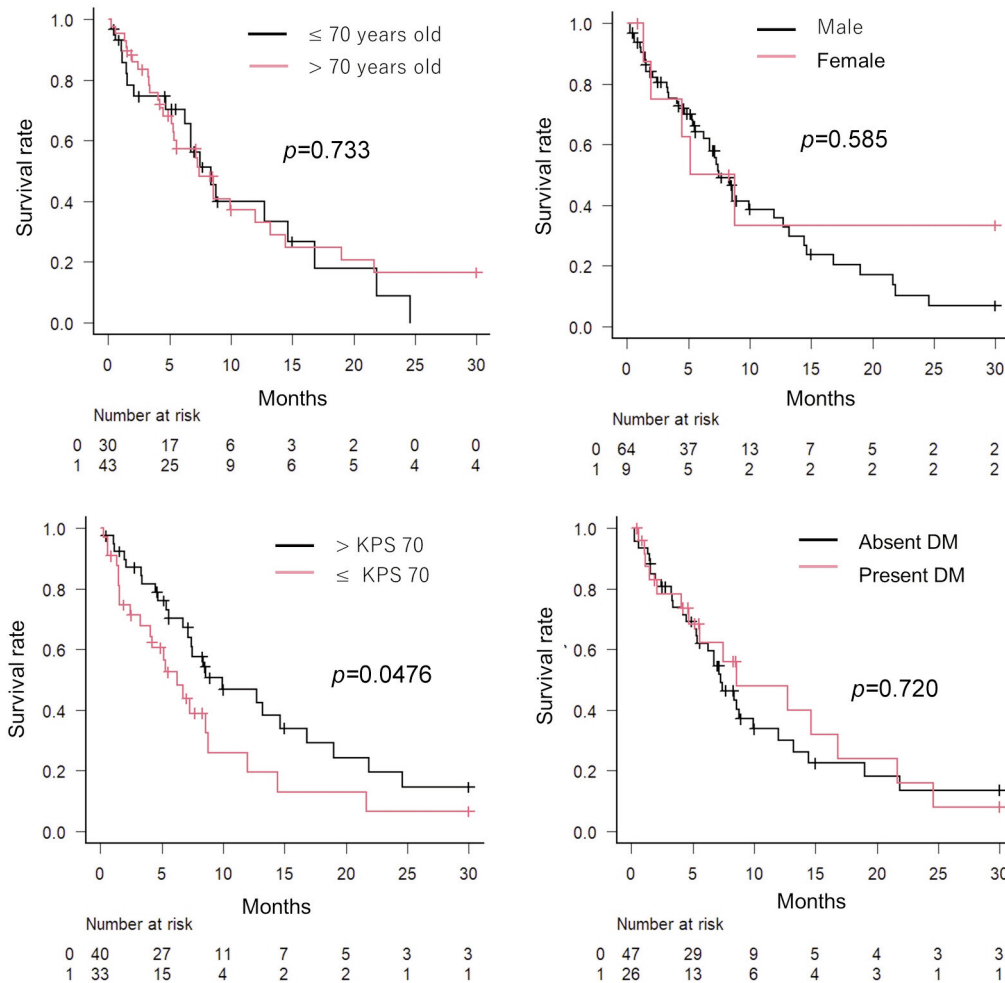


Figure 1. Kaplan–Meier survival curves for overall survival categorized by patients’ age (A), sex (B), Karnofsky performance status (KPS) (C), and presence of distant metastasis (DM) (D).

Table II. Multivariate hazard ratios by Cox regression analysis of overall survival.

Variables		Hazard ratio	95% Confidence interval	p-Value
Age	≤ 70 years	1		
	> 70 years	0.818	0.447-1.496	0.513
Sex	Male	1		
	Female	0.638	0.253-1.610	0.341
Karnofsky performance status	≤ 70	1		
	> 70	1.949	1.062-3.578	0.031
Distant metastasis	Absent	1		
	Present	0.817	0.429-1.555	0.537

of 3.7 Gy administered twice daily, repeated every 3-4 weeks (16). Choudhary *et al.* reported that the QUAD SHOT regimen stands out as a highly effective hypofractionated palliative radiotherapy schedule, offering superior benefits

when compared with the conventional approach of 30 Gy delivered over 10 fractions within two weeks (17). Murthy *et al.* evaluated a twice-weekly palliative radiotherapy regimen of 32 Gy delivered over eight fractions and reported

significant improvement in pain and anxiety levels, minimal side effects, and a median survival period of 5.5 months (18).

One of the key observations from this study was the suitability of palliative radiotherapy in older patients with HNSCC. The treatment of older adults with cancer, particularly in palliative care, involves various considerations. Our results revealed that a subset of older patients had similar OS rates than those of others. Rühle *et al.* investigated palliative radiotherapy for bone metastases in octogenarian patients with cancer (19). Their findings indicated that age itself is not a prognostic factor for OS in these patients who are receiving palliative radiotherapy. A novel validated prognostic score was proposed based on clinical data allowing the stratification between prognostic groups of older patients with HNSCC (20). In the treatment of older patients, individualized, careful, and comprehensive assessments are necessary. Moreover, the integration of supportive care measures, such as pain management and nutritional support, proved instrumental in enhancing the overall well-being of patients, aligning with the principles of palliative care.

In summary, in this single-center retrospective study, we analyzed the clinical outcomes of palliative radiotherapy in patients with HNSCC. Our results indicated that for the older population, palliative radiotherapy outcomes were comparable to those of the younger population, suggesting that age does not significantly diminish treatment efficacy. Palliative radiotherapy could be a crucial intervention for older patients, ensuring the preservation of their quality of life and overall well-being. Comprehensive geriatric assessments in the treatment of older patients are also important. Thus, further research in this area is imperative. By refining radiation treatment protocols, we can optimize outcomes and enhance the overall well-being of older patients undergoing palliative radiotherapy for HNSCC. Such advancements are crucial in improving the lives of these patients and ensuring that they receive the best possible care tailored to their specific needs.

Conflicts of Interest

The Authors affirm that there are no competing interests concerning this study.

Authors' Contributions

A.K. conceived and designed the study. Data acquisition was carried out by A.K., M.M., G.T., O.S., and H.Y. Data analysis and interpretation were conducted by A.K., M.M., G.T., O.S., and H.Y. A.K. drafted the manuscript, which was subsequently reviewed and approved by all Authors.

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