Cancer Management and Research

Open Access Full Text Article

ORIGINAL RESEARCH

Hypopharyngeal Squamous Cell Carcinoma in Elderly Patients Aged ≥70 Years: Surgery and Postoperative Radiotherapy Improves Outcomes in Selected Patients

Ru Wang[1,*], Ahmad A Hariri[2,*], Hengmin Tao[1], Yumei Wei[1], Zhenghua Lyu[3]

[1]Department of Head and Neck Radiotherapy, Shandong Provincial ENT Hospital, Shandong University, Jinan, Shandong, People's Republic of China; [2]Department of Otolaryngology-Head and Neck Surgery, London North West University Healthcare NHS Trust, London, England, UK; [3]Department of Otolaryngology-Head and Neck Surgery, Shandong Provincial ENT Hospital, Shandong University, Jinan, Shandong, People's Republic of China

*These authors contributed equally to this work

Correspondence: Yumei Wei; Zhenghua Lyu, Email 15553119268@163.com; entlvzhenghua@163.com

Objective: To summarize the efficacy of surgery plus postoperative radiotherapy as initial treatment in elderly patients aged ≥70 years with advanced hypopharyngeal cancer and to analyze prognostic factors.

Methods: Retrospective analysis of 77 elderly patients aged ≥70 years with stage III–IV hypopharyngeal squamous cell carcinoma who underwent surgery as initial treatment at Shandong Provincial ENT Hospital between 2006–2020. Treatment completion rate and prognostic factors were summarized and analyzed, with comparisons made to non-surgical treatments in published literature. SPSS 26.0 was used for analysis. Univariate Cox regression analysis was applied to identify potential predictors of overall survival (OS) and disease-free survival (DFS). Kaplan–Meier method with Log rank test was used to calculate and compare survival rates. Multivariate analysis employed the Cox proportional hazards regression model, with $P < 0.05$ considered statistically significant.

Results: The study achieved 100% follow-up with a median duration of 62 months. Among the cohort, 26 patients received surgery only whilst 51 received surgery plus radiotherapy, seven patients failed to complete radiotherapy resulting in a completion rate of 86.27%. Survival analysis revealed significant intergroup differences: at 1 year, OS/DFS rates were 76.9%/73.1% in Group A versus 93.2%/81.8% in Group B (both $P < 0.05$). By 3 years, OS/DFS rates were 61.5%/57.7% in Group A versus 77.3%/70.5% in Group B. The overall 3-year and 5-year OS rates for the cohort were 68.8% and 52.3%, respectively. Univariate analysis showed no significant differences in gender, age, T/N staging, comorbidities, or second primary malignancies (all *P* > 0.05), but treatment modality was a significant predictor of both OS ($P = 0.002$) and DFS ($P = 0.001$). Multivariate COX regression analysis confirmed N staging and treatment modality as independent prognostic factors for OS ($P = 0.007$ and 0.002, respectively) and DFS (P = 0.009 and 0.002, respectively).

Conclusion: Elderly hypopharyngeal cancer patients tolerated surgery and postoperative radiotherapy well. Active pursuit of comprehensive treatment is recommended for fit stage III–IV patients aged ≥70 years to improve outcomes.

Keywords: hypopharyngeal neoplasms, squamous cell carcinoma, aged, radiotherapy, prognosis

Introduction

Against the backdrop of increasing tobacco[1] and alcohol consumption,[2] rising human papilloma virus (HPV) infection prevalence,[3] and global population aging, the incidence of head and neck squamous cell carcinoma (HNSCC) in older adults has demonstrated a clear upward trend.[4] Epidemiological evidence indicates that approximately 30% of current HNSCC cases involve patients aged ≥70 years,[5] with over 50% being ≥60 years old.[6] This trend reflects the combined impact of modifiable risk factors and demographic shifts, underscoring the need for age-tailored oncology management strategies.

Hypopharyngeal cancer exhibits the poorest prognosis among head and neck tumors, accounting for 3–5% of HNSCC cases.[7] Due to its insidious onset, submucosal infiltration, and atypical symptoms, 70–85% of patients are diagnosed at

Received: 29 April 2025
Accepted: 11 July 2025
Published: 26 July 2025

stage III–IV. Multidisciplinary treatment remains the standard of care for locally advanced hypopharyngeal cancer. The current *National Comprehensive Cancer Network (NCCN)* guidelines outline 2 primary treatment modalities: radical laryngectomy ± (stage-dependent) postoperative radio(system)therapy, and radical or induction radio(system)therapy. Surgery-based approaches typically require total laryngectomy/partial laryngopharyngectomy, which is associated with surgical risks and impairs phonation, deglutition, and pulmonary ventilation. Radical or induction radio(system)therapy carries the risk of delaying radical surgery due to radio/chemoresistance, potentially compromising oncologic control and functional preservation.

Current research on managing geriatric hypopharyngeal cancer patients remains scarce, with treatment strategies still debated. Compared to younger counterparts, older adults often have higher comorbidity burdens and reduced tolerance to aggressive interventions, increasing postoperative complication risks.[8] Consequently, they are frequently deemed unsuitable for surgery or excluded from surgical candidacy in clinical decision-making. Through a retrospective survival analysis of 77 cases and comparative analysis with non-surgical treatment data from the literature, this study seeks to offer further insights into surgical management for elderly hypopharyngeal cancer patients.

Materials and Methods

Data Collection

A retrospective analysis was performed on 77 patients aged ≥70 years with stage III–IV hypopharyngeal squamous cell carcinoma treated at Shandong Provincial ENT Hospital between January 2006 and January 2020. Patients were classified into three groups based on treatment: surgery alone (Group A), surgery with postoperative radiotherapy (Group B), and surgery with incomplete postoperative radiotherapy (Group C). Inclusion criteria: 1) surgical treatment with postoperative pathological confirmation of hypopharyngeal squamous cell carcinoma; 2) age ≥ 70 years; 3) newly diagnosed primary tumor; 4) stage III–IV disease; 5) Eastern Cooperative Oncology Group (ECOG) performance status 0–1. Exclusion criteria: 1) distant metastases; 2) prior neck surgery or chemoradiotherapy. Tumors were staged according to the 8th edition of the American Joint Committee on Cancer (AJCC) TNM classification.[9]

Preoperative evaluation included electronic laryngoscopy with Valsalva maneuver to visualize the post-cricoid region and esophageal inlet, supplemented by narrow-band imaging (NBI) to assess mucosal carcinomatous changes. Gastroscopy was routinely performed to detect second primary tumors. Preoperative staging included contrast-enhanced neck computed tomography (CT)/ magnetic resonance imaging (MRI),[10] for tumor invasion depth, contrast-enhanced chest CT to exclude mediastinal/lung metastases, abdominal ultrasound/CT for hepatic metastases, and 99mTc-methylene diphosphonate bone scintigraphy for osseous metastases. 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT)[11] or PET/MRI[12] was used for indeterminate cases.

All patients were evaluated by the multidisciplinary team (MDT) and determined to be ineligible for endoscopic resection or refused neoadjuvant therapy due to T/N stage, local invasion site, or lymph node metastasis. Surgery was the current preferred potential curative modality.

Treatment

Surgery

All procedures were performed by a specialized surgical team. Approaches included partial hypopharyngectomy, partial laryngectomy + partial hypopharyngectomy, total laryngopharyngectomy, and total laryngopharyngectomy + cervical esophagectomy. Reconstruction methods (free jejunal transplantation, gastric pull-up, pectoralis major myocutaneous flap) were tailored to defect size. Standardized central neck dissection was performed. For T3–T4N0 cases, bilateral selective neck dissection (levels II–IV) was conducted. N1/N2a cases underwent modified/extended neck dissection (levels II–V) on the positive side and selective dissection (levels II–IV) on the contralateral side. N2b/N2c cases required bilateral modified/extended neck dissection (levels II–V).

Postoperative Radiotherapy

Intensity-modulated radiotherapy (IMRT) was initiated 4–6 weeks postoperatively based on final pathology. Indications included close margins (<1–3 mm), advanced T stage (T3–T4), positive margins, nodal positivity, peri-nodal extension

(PNE), peri-neural invasion (PNI), lymphovascular embolization (LVE), and poorly differentiated squamous cell carcinoma (PDSCC). A conventional fractionation schedule was used: 2 Gy/fraction, 5 days/week, totaling 50 Gy in 25 fractions, with high-risk areas boosted to 60 Gy.

Follow-Up

Systematic follow-up included outpatient visits, inpatient evaluations, and telephone interviews. DFS was defined as the time interval from the date of initial diagnosis to tumor recurrence, metastasis, or death from any cause. DFS was assessed via imaging (neck MRI/CT every 12 weeks, contrast-enhanced chest/abdominal CT for distant metastases, PET-CT for ambiguous cases) and gastroscopy every 6 months for second primaries. Clinical assessments included physical exams and laryngoscopy. Recurrence/progression were confirmed by histology or repeat imaging.

Acute/chronic radiotherapy toxicities were evaluated using Common Terminology Criteria for Adverse Events (CTCAE, v5.0), with weekly assessments during radiotherapy and annual reviews post-treatment.

Variables and Statistical Analysis

Variables included age, gender, T/N stage, AJCC stage, comorbidities, second primaries, treatment, surgical type, OS, and DFS (primary endpoints). Data were analyzed using SPSS 26.0. Categorical variables were analyzed using the chi-square test (χ^2-test), and Fisher's exact test was used if the expected frequency in any cell was <5. Univariate Cox regression identified survival predictors. Kaplan–Meier method with Log rank test compared survival rates. Multivariate analysis used the Cox proportional hazards model, with $P < 0.05$ indicating significance.

Results

Clinical Characteristics and Survival Outcomes

Cutoff date was March 1, 2025. The cohort comprised 70 males and 7 females (aged 71–81 years, mean 73 years), including 24 ≥75 years and 53 <75 years. Primary tumor locations: pyriform sinus (63), posterior pharyngeal wall (10), post-cricoid region (4). Comorbidities were present in 39 patients (hypertension, diabetes, coronary artery disease, etc). Staging: 26 stage III, 51 stage IV. Median follow-up was 62 months with 100% completion. Overall, 3-year and 5-year OS rates were 68.8% and 52.3%, respectively. Group A (surgery alone) had 1-year/3-year OS/DFS rates of 76.9%/73.1% and 61.5%/57.7%, versus 93.2%/81.8% and 77.3%/70.5% in Group B (surgery + radiotherapy) (Table 1).

Basic Characteristics and Statistical Analysis of Subgroups

There were no significant differences in AJCC staging, T/N staging, or surgical type between Group A and Group B (P > 0.05), indicating that the two groups were comparable. (Table 2).

Univariate Analysis

No significant survival differences were observed for gender, age, T stage, comorbidities, or second primaries (all P > 0.05). Treatment modality was a significant predictor of OS (P=0.002) and DFS (P=0.001) (Table 3, Figure 1).

Table 1 OS and DFS of Elderly Patients with Hypopharyngeal Cancer

Variable	Surgery Only (%)	Surgery with Complete RT (%)	Surgery with Incomplete RT (%)
OS (1 yr)	76.9	93.2	71.4
DFS (1 yr)	73.1	81.8	42.9
OS (3 yr)	61.5	77.3	42.9
DFS (3 yr)	57.7	70.5	42.9
OS (5 yr)	44.4	63.5	28.6
DFS (5 yr)	40.7	62.4	28.6

Abbreviations: OS, overall survival; DFS, disease-free survival; RT, postoperative radiotherapy.

https://doi.org/10.2147/CMAR.S529332

Table 2 Basic Characteristics and Statistical Analysis of Subgroups

Variable	Group A (n = 26)	Group B (n = 44)	Group C (n = 7)	Statistical Test	P
Histopathological subtype	Squamous cell carcinoma (100%)	Squamous cell carcinoma (100%)	Squamous cell carcinoma (100%)	–	–
AJCC stage				Chi-square test	0.689
- III	10 (38.5%)	16 (36.4%)	0 (0%)		
- IV	16 (61.5%)	28 (63.6%)	7 (100%)		
T stage				Fisher's exact test	0.892
- T1-T2	5 (19.2%)	9 (20.5%)	1 (14.3%)		
- T3-T4	21 (80.8%)	35 (79.5%)	6 (85.7%)		
N stage				Chi-square test	0.743
- N0-1	13 (50.0%)	18 (40.9%)	3 (42.9%)		
- N2-3	13 (50.0%)	26 (59.1%)	4 (57.1%)		
Surgical type				-	-
-Partial hypopharyngectomy	8 (30.8%)	14 (31.8%)	2 (28.6%)		
-Total laryngopharyngectomy	18 (69.2%)	30 (68.2%)	5 (71.4%)		
Completion status of postoperative radiotherapy	-	Completed (44/44, 100%)	Incomplete (7/7, 100%)	Fisher's exact test	**<0.001***
Radiation dose (Gy)	-	50-60 (median 54)	0-40 (Incomplete)	-	-

Note: *Indicates statistically significant differences between groups (P < 0.05).
Abbreviations: Group A, surgery alone; Group B, surgery with postoperative radiotherapy; Group C, surgery with incomplete postoperative radiotherapy.

Table 3 Patient Characteristics and Univariate Analysis of Survival-Associated Factors in Elderly Patients with Hypopharyngeal Cancer

Variable	Total	Death (%)	*P* (OS)	*P* (DFS)
Gender			0.565	0.586
Male	70	49(70.00)		
Female	7	4(57.14)		
Age (years)			0.570	0.489
70 (incloud 70) −75	53	32(60.38)		
75 (incloud 75) −80	18	16(88.89)		
≥80	6	5(83.33)		
T stage			0.216	0.159
T1-2	14	7(50.00)		
T3-4	63	46(73.02)		
N stage			0.136	0.149
N0-1	34	22(64.71)		
N2-3	43	31(72.09)		
AJCC stage			0.344	0.311
III	26	17(65.38)		
IV	51	36(70.59)		
With basic diseases			0.545	0.563
No	38	24(63.16)		
Yes	39	29(74.36)		
With other primary tumors			0.444	0.471
No	64	43(67.19)		
Yes	13	10(76.92)		

(*Continued*)

Table 3 (Continued).

Variable	Total	Death (%)	*P* (OS)	*P* (DFS)
Treatment			**0.002**	**0.001**
Surgery only (Group A)	26	24(92.31)		
Surgery with Complete RT (Group B)	44	22(50.00)		
Surgery with Incomplete RT (Group C)	7	7(100.00)		

Note: P value in bold means statistically significant.
Abbreviations: OS, overall survival; DFS, disease-free survival; RT, postoperative radiotherapy; AJCC, American Joint Committee on Cancer.

Multivariate Analysis

N staging (P=0.007) and treatment modality (P=0.002) were independent OS predictors, with similar significance for DFS (P=0.009 and 0.002, respectively). N0–1 patients had better outcomes than N2–3, and Group B outperformed Group A (Table 4, Figure 2).

Radiotherapy Tolerance

All patients experienced grade 1–2 mucositis (no grade ≥ 3). Grade 1–2 dermatitis occurred in 38 patients (74.5%), with no severe skin toxicity. Mild myelosuppression (grade 1–2) was noted in 12 patients (23.5%), with no grade ≥ 4 hematological events. Seven patients (13.7%) discontinued radiotherapy early due to postoperative complications (pneumonia, pharyngocutaneous fistula, etc.), unrelated to radiation toxicity.

At 1-year follow-up, 22 patients (43.1%) reported mild dysphagia (surgery-related), with no severe stenosis. Grade 2 xerostomia occurred in 18 patients (35.3%), and mild cervical lymphedema in 15 (29.4%). Three patients (5.9%) developed metachronous primaries (2 esophageal SCC, 1 lung adenocarcinoma), detected via screening.

Cause of Death Analysis

Time from symptom onset to diagnosis ranged from 2 weeks to 1 year. The 1-year and 3-year OS rates were 87% and 68.8%, respectively. Of 54 deaths, causes included local recurrence (1, 2.3%), regional nodal recurrence (5, 11.9%), distant metastasis (20, 37.0%), perioperative mortality (1, 2.3%), second primaries (3, 7.1%), and other causes (24, 57.1%).

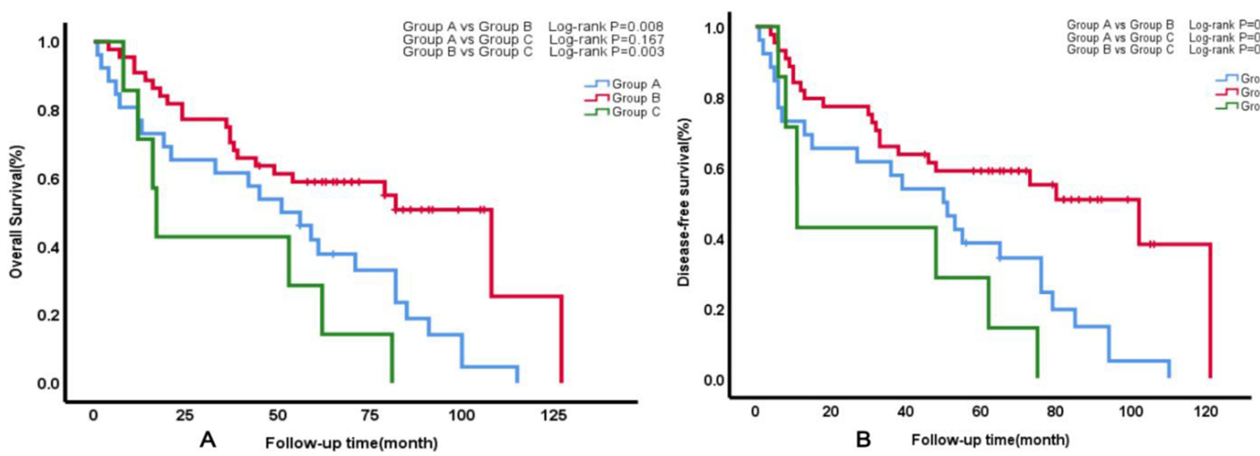

Figure 1 Results of univariate analysis (**A**): The KM curve of OS; (**B**): The KM curve of DFS.
Abbreviation: OS, overall survival; DFS, disease-free survival; Group A, surgery alone; Group B, surgery with postoperative radiotherapy; Group C, surgery with incomplete postoperative radiotherapy.

https://doi.org/10.2147/CMAR.S529332

Table 4 Multivariate Cox Proportional Hazards Model Analysis for OS and DFS in Elderly Patients with Hypopharyngeal Cancer

Variable	B	SE	Wald	*P*	HR (95% CI)
OS					
N stage					
N0-1					1.000
N2-3	0.819	0.305	7.192	**0.007**	2.268(1.247–4.126)
Treatment					
Group A					1.000
Group A vs Group B	−0.943	0.310	9.260	**0.002**	0.389(0.212–0.715)
Group A vs Group C	0.617	0.444	1.929	0.165	1.853(0.776–4.425)
DFS					
N stage					
N0-1					1.000
N2-3	0.795	0.303	6.894	**0.009**	2.215(1.223–4.011)
Treatment					
Group A					1.000
Group A vs Group B	−0.977	0.311	9.880	**0.002**	0.377(0.205–0.692)
Group A vs Group C	0.552	0.442	1.556	0.212	1.736(0.730–4.131)

Note: P value in bold means statistically significant.
Abbreviations: OS, overall survival; DFS, disease-free survival; CI, confidence interval; B, coefficient; SE, standard error; Wald, wald statistic; HR, hazard ratio.

Discussion

The aging population is reshaping cancer treatment paradigms. Age-related physiological decline becomes more pronounced after 70 years, often accompanied by increased comorbidities.[13,14] Elderly patients typically exhibit higher burdens of medical comorbidities and poorer performance status, which have fueled debates on optimal treatment strategies. They are frequently deemed unsuitable for intensive multimodality therapy, tend to present with advanced-

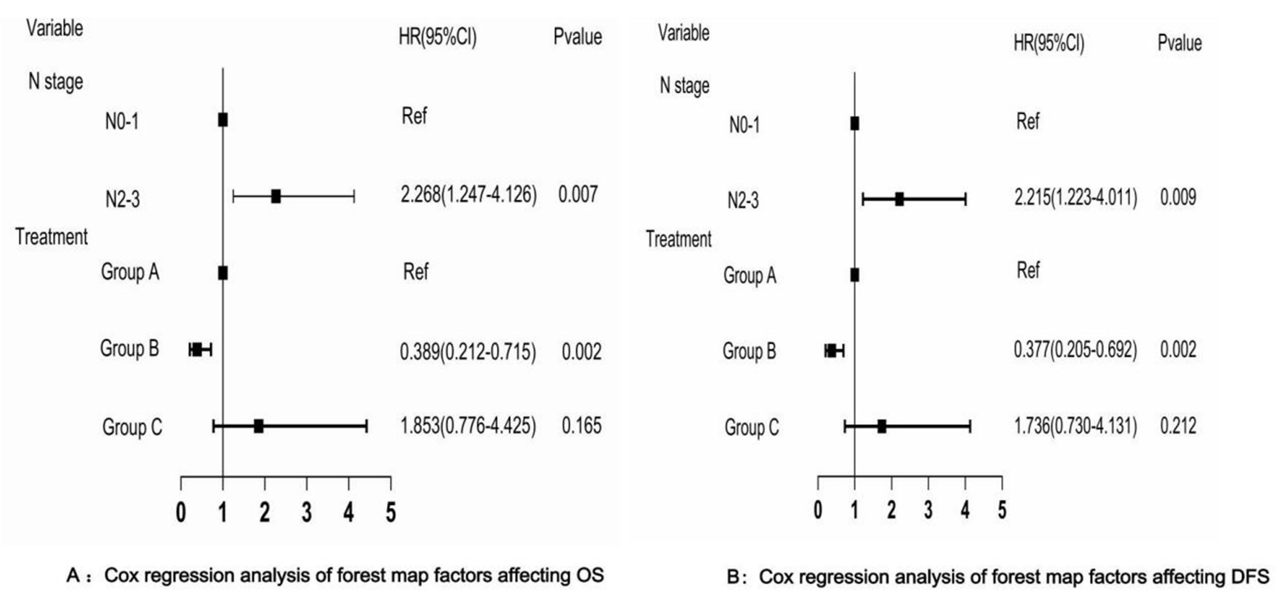

Figure 2 Results of multivariate COX analysis: (**A**): Cox regression analysis of forest map factors affecting OS; (**B**): Cox regression analysis of forest map factors affecting DFS.
Abbreviation: OS, overall survival; DFS, disease-free survival; Group A, surgery alone; Group B, surgery with postoperative radiotherapy; Group C, surgery with incomplete postoperative radiotherapy.

stage disease, receive monotherapy, and have low rates of recurrence-directed retreatment. Despite these clinical challenges, the geriatric oncology literature remains scarce, particularly for hypopharyngeal cancer in patients aged ≥70 years.

In this study, we compared the survival outcomes between a surgery-alone group and a surgery-combined-with-radiotherapy group in a cohort of patients aged ≥70 years with locally advanced hypopharyngeal cancer. The results showed that the combined treatment modality (surgery + radiotherapy) was well-tolerated in this population and had significant survival advantages over surgery alone. Considering the limited number of hypopharyngeal cancer cases in patients over 70 years old and the difficulty of obtaining concurrent non-surgical control groups in real-world clinical practice, this study compared by integrating domestic literatures on hypopharyngeal cancer across all age groups (Table 5) and referred to clinical research data of large-scale non-surgical treatments (Table 6). It was further found that the elderly subgroup receiving surgical treatment still showed good clinical benefits.

Table 5 Comparison of Treatment Outcomes Between This Study and Domestic Literatures in Hypopharyngeal Cancer

Trial	Year	No.	Age (Years)	Anatomic Subsite	Stage (n)	Treatment Arms (n)	OS (%)
Ping Zhang Tang.[15]	2004	464	20-88 (average 56.3)	Hypopharynx	I(l0) II(26) III(129) IV(299)	Preoperative RT →S(202) S→Postoperative RT (22) S only (26) Salvage surgery followed failed radical RT (40) Radical RT (174)	Preoperative RT →S 46.3% (5 yr) S→Postoperative RT 49.2% (5 yr) S only 22.8% (5 yr) Salvage surgery followed failed radical RT 40.8% (5 yr) Radical RT 18.0% (5 yr)
Wei Xu.[16]	2018	264	36-81 (Median age 58)	Hypopharynx	I(2) II(14) III(32) IV(216)	Preoperative RT→S(8) S→Postoperative RT (229) S→Postoperative CCRT (13) S only (14)	62.8% (3 yr), 51.3% (5 yr)
YiLu.[17]	2019	321	35-82 (16patients were ≥71 years)	Hypopharynx	I(5) II(11) III(104) IV(143)	S→Postoperative comprehensive therapy (197) Nonsurgical treatment (124)	49.39% (3 yr), 41.38% (5 yr)
Lei Tao.[18]	2021	229	<60 (122); ≥60 (107)	Hypopharynx	T3-T4	S→Postoperative RT (57) S→Postoperative CCRT (76) Surgery only (96)	39.07% (3 yr), 29.03% (5 yr)
This trial	2024	77	≥70	Hypopharynx	III–IV	S→Postoperative RT (44) S only (26)	68.8% (3 yr), 52.3% (5 yr)

Abbreviations: CCRT, concurrent chemoradiotherapy; RT, radiotherapy; S, surgery; OS, overall survival.

Table 6 Comparison of OS Between This Study and Non-Surgical Treatment Studies in HNSCC

Trial	Year	No.	Stage	Anatomic Subsite	Treatment Arms (n)	OS (%)
RTOG 91–11[19]	2003	518	Stage III-IV	Larynx	PF→RT (CR/PR) PF→S (not reached CR/PR) (173)	58.1% (5 yr)
					CCRT (172)	55.1% (5 yr)
					RT (173)	55.1% (5 yr)
EORTC 24954[20]	2009	450	Stage III-IV (T2-4N0~2)	Larynx	Sequential therapy: PF→RT (224)	48.5% (5 yr)
					Alternating therapy: (PF→20 Gy RT) ×3→ PF (226)	51.9% (5 yr)
GORTEC 2000–01[21]	2009	213	Stage III-IV	Larynx and hypopharynx	PF→RT (CR/PR) PF→S (not reached CR/PR) (103)	60.0% (3yr)
					TPF→RT (CR/PR) TPF→S (not reached CR/PR) (110)	60.0% (3yr)
TAX 324[22]	2009	166	Stage III-IV	Larynx and hypopharynx	PF+CCRT (76)	40.0% (3yr)
					TPF+CCRT (90)	57.0% (3yr)
This trial	2023	77	Stage III-IV	Hypopharynx	S (26)	40.7% (5 yr)
					S→RT (44)	62.4% (5 yr)

Abbreviations: HNSCC, head and neck squamous cell carcinoma; CCRT, concurrent chemoradiotherapy; RT, radiotherapy; S, surgery; TPF, docetaxel, cisplatin, and fluorouracil; PF: cisplatin and fluorouracil; CR, complete response; PR, partial response; OS, overall survival; RTOG, radiation therapy oncology group; EORTC, European Organization for Research and Treatment of Cancer; GORTEC, Groupes Oncologie Thorax et Céphale-Vaisseau; TAX, Taxane - based therapy.

Amini et al[23] compared 4,042 non-metastatic head and neck cancer patients aged >70 years receiving chemoradiotherapy vs radiotherapy alone (1,320 oropharynx, 2,045 larynx, 677 hypopharynx). Over 70% had a Charlson-Deyo comorbidity score of 0, with median survival of 21.9 months and 2-/5-year OS rates of 48.0%/24.5%. Chemoradiotherapy improved OS vs radiotherapy alone in patients < 81 years with low Charlson comorbidity index (CCI) and T1-2/N2-3 or T3-4/N0-3 disease. However, two 71–80-year-old subgroups showed no OS benefit: (1) T3-4, N1-3, Charlson ≥ 1; (2) T1-2, N1, Charlson 0–1, likely due to increased toxicity in elderly/comorbid patients. Maurer[24] analyzed 193 stage III–IVB head and neck tumor patients (102 laryngeal, 91 hypopharyngeal) from the Regensburg registry: 68 underwent radical laryngectomy ± adjuvant chemoradiotherapy, and 125 received radical/induction chemoradiotherapy. Median OS was 36.6 months (surgical), 29.3 months (non-surgical), and 31.2 months (overall), with no significant OS/PFS differences between groups. Our elderly hypopharyngeal cancer patients received surgery ± postoperative radiotherapy without chemotherapy (a median duration of 62 months). Perioperative mortality within 6 months occurred in 4 patients: two due to acute cardiovascular and cerebrovascular events, and two due to poor nutrition with gradual weakness and cachexia. Most patients, however, tolerated surgery, with 5-year survival rates of 40.7% in the surgery-only group and 62.4% in the surgery-plus-postoperative radiotherapy group.

Studies on hypopharyngeal cancer in patients aged ≥70 years remain limited. Sanabria et al[25] evaluated 242 elderly (≥70 years) head and neck cancer surgical patients, revealing 87.6% had comorbidities, with 56.6% experiencing postoperative complications (44.6% local, 28.5% systemic). Preoperative comorbidities were associated with increased postoperative complications. Kowalski et al[26] retrospectively analyzed 115 elderly (>70 years, 70–84 years) head and neck cancer patients undergoing curative surgery, matched with 115 younger controls (10–69 years). No significant differences were observed between groups in postoperative complications, mortality, or recurrence rates. Non-cancer causes contributed to lower 5-year survival in the elderly (43% vs 56%, p = 0.10). Our study showed no impact of comorbidities on univariate analysis, likely due to most patients having mild comorbidities (only three with three comorbid conditions). No survival difference was found by second malignancy, possibly because other malignancies occurred earlier and at lower stages. Our 5-year survival rate of 52.3% is consistent with published literature.

Schroeff et al[27] followed 266 elderly (>70 years) and younger (45–60 years) HNSCC patients over 3–6 years, identifying advanced stage, increased comorbidities, and non-standard treatment as independent predictors of poorer survival in elderly patients. Our multivariate analysis confirmed significantly better OS and DFS in N0–1 vs N2–3 patients, consistent with prior studies. No significant association was found for T stage, possibly due to the small sample size in the T1–2 subgroup.

A study[28] compared radiotherapy tolerance between 452 elderly (≥75 years) and 1860 younger (<75 years) HNSCC patients. Among those receiving definitive radiotherapy, treatment interruptions, completion rates, and treatment-related mortality did not differ significantly between groups (238 elderly vs 1249 younger). In a chemoradiotherapy subset (39 elderly vs 621 younger), unplanned interruptions occurred in 22% vs 25% (P = 0.612), with non-completion rates of 4% vs 7% (P = 0.498). Another study[29] evaluated 85 younger (<70 years) and 27 elderly (≥70 years) patients treated with IMRT/IGRT, showing no significant differences in treatment failure (9.7% vs 4.2%, P = 0.58), protocol deviations, or survival. Notably, our study's postoperative radiotherapy non-completion rate (12.9%) exceeded prior reports, likely due to elderly patients' poorer functional status and treatment-related toxicities.

Beyond their established carcinogenic effects, severe systemic comorbidities (pulmonary, cardiovascular, hepatic, metabolic) significantly correlate with poorer patient prognosis.[30] A multifaceted metric integrating comorbidity and age has proven valuable in prognosing various cancers.[31–33] In our institutional practice, patients with an ECOG performance status ≥ 2 typically cannot tolerate radical surgery or concurrent chemoradiotherapy, instead receiving radiotherapy or targeted therapies (eg, nimotuzumab, anlotinib hydrochloride capsules, cetuximab). Those with an ECOG score ≥ 3 are managed solely with palliative and supportive care.

This study has limitations. As a single-center retrospective analysis of 77 hypopharyngeal cancer patients, selection bias is inherent. While radiotherapy toxicities were tracked, the focus on survival and high non-cancer mortality hindered chronic toxicity analysis. The absence of chemotherapy users leaves its role unclear, and concurrent chemoradiotherapy benefits for fit elderly patients require validation. The cohort comprised mainly mild-to-moderate comorbidity patients, limiting generalizability to frail or unresectable cases. Despite superior survival vs historical controls, cross-study variability in comorbidities and tumor stage may confound comparisons. Multicenter prospective studies are needed to assess comorbidity burden and treatment responses, clarifying combined modality benefits in elderly patients.

Conclusion

For fit elderly patients (≥70 years) with stage III–IV hypopharyngeal cancer, combined surgery and radiotherapy is well-tolerated and improves survival. Clinicians should abandon ageist biases and actively consider comprehensive treatment to optimize outcomes.

Abbreviations

OS, overall survival; DFS, disease-free survival; HPV, human papilloma virus; HNSCC, head and neck squamous cell carcinoma; NCCN, National Comprehensive Cancer Network; MDT, multidisciplinary team; CCRT, concurrent chemoradiotherapy; ECOG, Eastern Cooperative Oncology Group; AJCC, American Joint Committee on Cancer; NBI, narrow-band imaging; CT, computed tomography; MRI, magnetic resonance imaging; IMRT, intensity-modulated radiotherapy; PNE, peri-nodal extension; PNI, peri-neural invasion; LVE, lymphovascular embolization; PDSCC, poorly differentiated squamous cell carcinoma; CTCAE, Common Terminology Criteria for Adverse Events; CCI, Charlson comorbidity index; IGRT, image-guided radiotherapy; RT, radiotherapy; SCC, squamous cell carcinoma; CI, confidence interval; B, coefficient; SE, standard error; Wald, wald statistic; HR, hazard ratio; S, surgery; TPF, docetaxel, cisplatin, and fluorouracil; PF, cisplatin and fluorouracil; CR, complete response; PR, partial response; RTOG, radiation therapy oncology group; EORTC, European Organization for Research and Treatment of Cancer; GORTEC, Groupes Oncologie Thorax et Céphale-Vaisseau; TAX, Taxane-based therapy.

Data Sharing Statement

The data of this study is available upon request from the correspondence author.

Ethics Approval and Consent to Participate

This study involving human participants was reviewed and approved by the Ethics Committee of Shandong Provincial ENT Hospital (no.2024-077-01). Confirming that all methods were performed under the relevant guidelines and regulations in the methods section and the informed consent was obtained from all participants or their respective legally authorized persons. All treatments were performed in accordance with the principles outlined in the Declaration of Helsinki.

Consent for Publication

All the authors agreed to publish the article.

Acknowledgments

All the researchers should be appreciated. This paper has been uploaded to Research Square as a preprint: https://www.researchsquare.com/article/rs-4223467/v1. For the newly submitted articles, we have added 18 months of tracking and summary, so the survival data have changed.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

Shandong Province medical health science and technology project (202409030379).

Disclosure

The authors report no conflicts of interest in this work.

References

1. Tsuzuki N, Wasano K, Kawasaki T, et al. The impact of second-hand smoke on ear, nose, and throat diseases and head and neck cancers in Japan: a cross-sectional study using a questionnaire and secondary data from the national health and nutrition survey. *Acta Otolaryngol*. 2021;141(11):1000–1004. doi:10.1080/00016489.2021.1989486
2. Di Credico G, Polesel J, Dal Maso L, et al. Alcohol drinking and head and neck cancer risk: the joint effect of intensity and duration. *Br J Cancer*. 2020;123(9):1456–1463. doi:10.1038/s41416-020-01031
3. Song C, Zhang SK, Qiao YL. Infection of human papillomavirus and head and neck cancer. *Zhonghua Zhong Liu Za Zhi*. 45(1):39–43. doi:10.3760/cma.j.cn112152-20211130-00884
4. van der Kamp MF, van Dijk BAC, Plaat BEC, et al. To what extent has the last two decades seen significant progress in the management of older patients with head and neck cancer? *Eur J Surg Oncol*. 2021;47(6):1398–1405. doi:10.1016/j.ejso.2021.01.014
5. Sikora AG, Toniolo P, DeLacure MD. The changing demographics of head and neck squamous cell carcinoma in the United States. *Laryngoscope*. 2004;114(11):1915–1923. doi:10.1097/01.mlg.0000147920.66486.bc
6. Gugić J, Primož P. Squamous cell carcinoma of the head and neck in the elderly. *Rep Pract Oncol Radiother*. 2012;18(1):16–25. doi:10.1016/j.rpor.2012.07.014
7. Takes RP, Strojan P, Silver CE, et al. Current trends in initial management of hypopharyngeal cancer: the declining use of open surgery. *Head Neck*. 2012;34(2):270–281. doi:10.1002/hed.21613
8. Polanczyk CA, Marcantonio E, Goldman L, et al. Impact of age on perioperative complications and length of stay in patients undergoing noncardiac surgery. *Ann Intern Med*. 2001;134(8):637–643. doi:10.7326/0003-4819-134-8-200104170-00008
9. American Joint Committee on Cancer. *AJCC Cancer Staging Manual*; 2017. https://link.springer.com/book/9783319406176.
10. Wu L-M, Xu J-R, Liu M-J. Value of magnetic resonance imaging for nodal staging in patients with head and neck squamous cell carcinoma: a meta-analysis. *Acad Radiol*. 2012;19(3):331–40.doi. doi:10.1016/j.acra.2011.10.027
11. Al-Ibraheem A, Abdlkadir AS, Shagera QA, et al. The diagnostic and predictive value of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography in laryngeal squamous cell carcinoma. *Cancers*. 2023;15(22):5461. doi:10.3390/cancers15225461
12. Al-Ibraheem A, Abdlkadir A, Herrmann K, et al. Diagnostic Accuracy of [18 F]FDG PET/MRI in head and neck squamous cell carcinoma: a systematic review and Metaanalysis. *J Nucl Med*. 2024;65(10):1533–1539. doi:10.2967/jnumed.124.268049
13. Derks W, Leeuw JR, Hordijk GJ, Winnubst JA. Differences in coping style and locus of control between older and younger patients with head and neck cancer. *Clin Otolaryngol*. 2005;30(2):186–192. doi:10.1111/j.1365-2273.2004.00938.x
14. Singh B, Alfonso A, Sabin S, et al. Outcome differences in younger and older patients with laryngeal cancer: a retrospective case-control study. *Am J Otolaryngol*. 2000;21(2):92–97. doi:10.1016/s0196-0709(00)85004-8
15. Zhang ZM, Tang PZ, Xu ZG, et al. Long-term results of different treatment modalities in 464 hypopharyngeal squamous-cell carcinoma patients. *Zhonghua Zhong Liu Za Zhi*. 2005;27(1):48–51.
16. Xu W, Lv ZH, Sha N, et al. Treatment and prognostic analysis of 264 cases of hypopharyngeal cancer. *Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi*. 2018;53(5):346–351. doi:10.3760/cma.j.issn.1673-0860.2018.05.004
17. Lu T, Li ZD, Li SC, et al. The clinical characteristics and two different treatment outcomes of 321 patients with hypopharyngeal squamous cell carcinoma. *Lin Chuang Er Bi Yan Hou Tou Jing Wai Ke Za Zhi*. 2019;33(3):275–279. doi:10.13201/j.issn.1001-1781.2019.03.022
18. Tao L, Zhou L, Zhang M, et al. Postoperative prognostic risk factors and treatment strategies for patients with T3-T4 hypopharyngeal squamous cell carcinoma. *Lin Chuang Er Bi Yan Hou Tou Jing Wai Ke Za Zhi*. 2021;35(5):400–404,409. doi:10.13201/j.issn.2096-7993.2021.05.004
19. Forastiere AA, Goepfert H, Maor M, et al. Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer. *N Engl J Med*. 2003;349(22):2091–2098. doi:10.1056/NEJMoa031317
20. Lefebvre JL, Rolland F, Tesselaar M, et al. Phase 3 randomized trial on larynx preservation comparing sequential vs alternating chemotherapy and radiotherapy. *J Natl Cancer Inst*. 2009;101(3):142–152. doi:10.1093/jnci/djn460
21. Janoray G, Pointreau Y, Garaud P, et al. Long-term results of a multicenter randomized Phase III trial of induction chemotherapy with cisplatin, 5-fluorouracil, ± docetaxel for larynx preservation. *J Natl Cancer Inst*. 2015;108(4):djv368. doi:10.1093/jnci/djv368
22. Posner MR, Norris CM, Wirth LJ, et al. Sequential therapy for the locally advanced larynx and hypopharynx cancer subgroup in TAX 324: survival, surgery, and organ preservation. *Ann Oncol*. 2009;20(5):921–927. doi:10.1093/annonc/mdn752
23. Amini A, Jones BL, McDermott JD, et al. Survival outcomes with concurrent chemoradiation for elderly patients with locally advanced head and neck cancer according to the national cancer data base. *Cancer* 2016;122(10):1533–1543. doi:10.1002/cncr.29956
24. Maurer J, Kuenzel J, Bohr C, et al. Laryngectomy plus postoperative radio(system)therapy versus primary radio(system)therapy for the treatment of locally advanced laryngeal and hypopharyngeal cancer – results from the University Clinical Cancer Registry Regensburg. *Acta Otolaryngol*. 2024;144(3):255–262. doi:10.1080/00016489.2024.2340086
25. Sanabria A, Carvalho AL, Melo RL, et al. Predictive factors for complications in elderly patients who underwent head and neck oncologic surgery. *Head Neck*. 2008;30(2):170–177. doi:10.1002/hed.20671
26. Kowalski LP, Alcantara PS, Magrin J, Parise Junior O. A case-control study on complications and survival in elderly patients undergoing major head and neck surgery. *Am J Surg*. 1994;168(5):485–490. doi:10.1016/s0002-9610(05)80107-2
27. Schroeff MP, Derks W, Hordijk GJ, Leeuw RJ. The effect of age on survival and quality of life in elderly head and neck cancer patients: a long-term prospective study. *Eur Arch Otorhinolaryngol*. 2007;264(4):415–422. doi:10.1007/s00405-006-0203-y
28. Huang SH, O'Sullivan B, Waldron J, et al. Patterns of care in elderly head-and-neck cancer radiation oncology patients: a single-center cohort study. *Int J Radiat Oncol Biol Phys*. 2011;79(1):46–51. doi:10.1016/j.ijrobp.2009.10.052
29. Nguyen NP, Vock J, Chi A, et al. Impact of intensity-modulated and image-guided radiotherapy on elderly patients undergoing chemoradiation for locally advanced head and neck cancer. *Strahlenther Onkol*. 2012;188(8):677–683. doi:10.1007/s00066-012-0125-0

30. Liu CT, Chiu TJ, Huang TL, Chien CY, Fang FM. Impact of comorbidity on survival for locally advanced head and neck patients treated by radiotherapy or radiotherapy plus chemotherapy. *Chang Gung Med J*. 2010;33(3):283–391.
31. Xue-Lian X, Hao. Cheng, Xin-Meng Wu, Jin-Hong Xu.The Naples Prognostic Score Exerts a Significant Impact on the Prognosis of Patients Diagnosed with External Auditory Canal Carcinoma After Surgery. *Cancer Manag Res*. 2025;25(17):985–996. doi:10.2147/CMAR.S527496
32. Cheng H, Xu JH, He JQ, Wu CC, Li JF, Xu XL. Nomogram based on immune-inflammatory indicators and age-adjusted Charlson comorbidity index score to predict prognosis of postoperative parotid gland carcinoma patients. *BMC Oral Health*. 2024;24(1):718. doi:10.1186/s12903-024-04490-5
33. Zhou S, Zhang XH, Zhang Y, Gong G, Yang X, Wan WH. The age-adjusted Charlson comorbidity index predicts prognosis in elderly cancer patients. *Cancer Manag Res*. 2022;14:1683–1691. doi:10.2147/CMAR.S361495