

Radiotherapy for hypopharyngeal carcinoma in Senegal: Experience of the main cancer care facility

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Abstract

Objectives: To describe the epidemiological, diagnostic, therapeutic, and prognostic factors associated with patients treated for hypopharyngeal carcinoma at the Radiotherapy Department of the National Hospital Center Dalal Jamm.

Patients and Methods: Data from 50 consecutive patients treated for hypopharyngeal carcinoma between 2018 and 2022 were retrospectively analyzed. All patients received three-dimensional conformal radiotherapy (3DCRT) with or without chemotherapy. Epidemiological and diagnostic data, treatment details, and therapeutic outcomes were collected in an Excel 2016 database created for the study. Statistical analyses were performed using SPSS version 20.0. Overall survival estimates were generated using the Kaplan-Meier method. Statistical significance was considered at $p = 0.05$. Uni- and multivariate analyses were conducted to identify prognostic factors associated with survival.

Results: The average age of the patients was 44 years (± 14.4 years), with a male-to-female ratio of 0.56. Sixteen percent of the patients were active smokers and 4% were alcohol consumers. The mean delay to the first consultation was 6 months, and dysphagia was the primary symptom (92%). The majority of patients (89.8%) were classified as stage IVa, and 10% had metastases at diagnosis. Treatment consisted of curative concurrent chemoradiotherapy (95.92%), preceded by induction chemotherapy in 58% of patients. A radiation dose of 70 Gy was utilized in 75% of cases. The 2-year overall survival rate was 25%. Multivariate analysis indicated that the presence of feeding gastrostomy ($p=0.044$), use of induction chemotherapy ($p=0.012$), and radiation dose less than 70 Gy ($p=0.020$) were associated with poorer survival.

Conclusion: Concurrent chemoradiotherapy using 3D conformal techniques improved management, although outcomes remain unsatisfactory. Prospective cohort studies are imperative to identify specific risk factors in our population. Additionally, timely access to appropriate treatment modalities could enhance prognosis.

Keywords: Cancer; Hypopharynx; Senegal; Radiotherapy; Chemotherapy

1. Introduction

Hypopharyngeal carcinoma accounts for 3% of head and neck cancers [1]. According to Globocan estimates in 2020, there were 86,257 new cases of hypopharyngeal cancer worldwide for both sexes, resulting in 40,902 deaths [2]. Asia has the highest incidence rate (52.2 per 100,000), followed by Europe (14.1 per 100,000). Incidence in Africa is

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relatively low at 1.34 per 100,000 population, with Africa ranking third in mortality, recording 1,376 deaths for both sexes [2].

In Senegal, hypopharyngeal carcinoma is the most common type of upper aerodigestive tract cancer in otolaryngology services based on hospital series [3,4]. These cancers are associated with multiple interconnected risk factors and often present at an advanced stage with early submucosal dissemination. They carry a poor prognosis due to significant lymphophilic and systemic metastatic potential [1].

Historically, treatment for hypopharyngeal cancer relied on radical surgical excision combined with postoperative radiotherapy or radiotherapy alone. Conservative treatments began to emerge with the development of laryngeal preservation procedures. Additionally, surgery for advanced stages is functionally debilitating, making laryngeal preservation strategies preferable as first-line treatment [1].

Our study aims to evaluate the profile and survival outcomes of patients with hypopharyngeal carcinoma treated with conformal radiotherapy at Dalal Jamm University Hospital Center.

2. Material and method

Between June 2018 and January 2022, 66 patients were treated for hypopharyngeal cancer at the radiotherapy department of Dalal Jamm Hospital. We included 50 patient records for this study based on the following criteria:

- Histologically proven squamous cell carcinoma of the hypopharynx
- Patients with an Eastern Cooperative Oncology Group (ECOG) performance status ≤ 3
- Patients who received curative or palliative radiotherapy
- Medical records containing patient information (age, sex, lifestyle, smoking, alcohol use, personal and family history), diagnosis (time from consultation to treatment initiation, symptoms, endoscopy findings, tumor size, staging), treatment details (radiotherapy, induction and concurrent chemotherapy), and outcomes (death, remission, loss to follow-up).

Patients were excluded if they had:

- History of previous cervical irradiation
- ECOG performance status > 3
- Incomplete dosimetry records

The ECOG performance status was used to assess the overall condition of patients.

Minimal patient evaluation included pan-endoscopy and cervical-thoracic CT scan for staging according to the TNM classification of the UICC 8th edition. Overall survival was defined as the time from the initial diagnostic date (biopsy) to the date of death or last follow-up. Data were collected in an Excel 2016 database created for the study. Statistical analyses were performed using SPSS version 20.0. Overall survival estimates were generated using the Kaplan-Meier method. Statistical significance was set at $p = 0.05$. Uni- and multivariate analyses were conducted to identify prognostic factors associated with survival.

3. Results

The median age of the patients was 46 years, ranging from 19 to 75 years. The age groups most represented were 50-60 years (24%, $n=12$) and 30-40 years (22%, $n=11$). Females constituted the majority (64%) with a male-to-female ratio of 0.56.

The median interval between symptom onset and initial consultation was 6 months. Clinical symptoms were predominantly dysphagia (92%) followed by odynophagia (50%). Sixteen percent of patients were smokers with an average consumption of 12 ± 13 pack-years. Endoscopy revealed an ulcerative or polypoid appearance of the tumor in 84.1% of cases. The median time from initial consultation to biopsy was 18 days (range: 1 to 364 days). Histological results were available more than 30 days after biopsy in 63.2% of cases. Squamous cell carcinoma was the histological type in all patients. Tumors were well-differentiated in 79.2% of cases, moderately differentiated in 18.8% of cases, and poorly differentiated in one patient. Tumor size was documented in 22 patients (44%), with a mean size of 42.1 mm and ranging from 11.3 to 218.16 mm. Upon staging, tumors were locally advanced with T3, T4, and positive nodal

involvement (N+) in 4.1% (n=3), 93.8%(n= 46) , and 57.1% (n=28) of cases, respectively. Ten percent of patients had metastases, with isolated pulmonary metastases in 4 patients and one patient presenting with secondary hepatic involvement. The main epidemiological and diagnostic characteristics of the patients are summarized in Table 1.

Table 1 Caractéristiques of the patients

Variable	Valeur
Age (years), median (IQR)	46 [19-75]
<i>Discovery Circumstances, n (%)</i>	
Dysphagia	46 (92%)
Odynophagia	25 (50%)
Adenopathy	19 (38%)
Weight loss	14 (28%)
Dyspnea	11 (22%)
Dysphonia	10 (20%)
Aphagia	7 (14%)
Reflex otalgia	2 (4%)
<i>ECOG Scale, n (%)</i>	
ECOG 0	1 (2%)
ECOG 1	34 (69,38%)
ECOG 2	13 (26,53%)
ECOG 3	1(2%)
<i>Medical History and Lifestyle, n (%)</i>	
Plummer-Vinson syndrome	2 (4%)
Previous ENT cancer	5 (10%)
Occasional alcohol use	2 (4%)
Active smoking	8 (16%)
<i>Histological Type, n (%)</i>	
Squamous cell carcinoma	50 (100%)
<i>Staging Evaluation, n (%)</i>	
Pan-endoscopy	48 (96%)
Cervico-thoracic CT scan	50 (100%)
<i>Stage Classification, n (%)</i>	
Stage III	2 (4,1%)
Stage IVA	44 (89,8%)
Stage IVC	3 (6,1%)

The interval between biopsy and initiation of treatment was specified in 19 cases. It averaged 68 ± 59.9 days, with a median of 50 days. Symptomatic treatments primarily included tracheostomy 32% (n=16), feeding gastrostomy 40% (n= 20), and occasionally nasogastric tube placement 12% (n= 6).

Neoadjuvant chemotherapy was administered to 58% of patients. The Carboplatin-Paclitaxel protocol was most commonly used (65.3%), followed by Cisplatin-5FU and Cisplatin-5FU-Taxotere protocols at 17.4% and 13%, respectively.

Table 2 Different chemotherapies used

Protocole	Fréquence (n)	Pourcentage (%)
PALCITAXEL-CARBOPLATINE	15	65,2
DOCETAXEL-CISPLATINE- 5 FU	3	13,0
CISPLATINE- 5 FU	3	13,0
DOCETAXEL-CARBOPLATINE- 5 FU	1	4,4
PACLITAXEL-CISPLATINE- 5 FU	1	4,4
Total	23	100,0

All patients underwent three-dimensional conformal radiotherapy (3DCRT). It was curative in 94.1% of cases and palliative in 6% of patients. The predominant dose level used was 70 Gy, administered in conventional 2 Gy fractions.

Various therapeutic and outcome aspects are summarized in Table 3 below.

Table 3 Treatment and evolution

Variable	Value
<i>Symptomatic Treatment, n (%)</i>	
Tracheostomy	16 (32%)
Feeding Gastrostomy	20 (40%)
Nasogastric Tube	6 (12%)
<i>Chemotherapy, n (%)</i>	
Neoadjuvant	29 (58%)
Concurrent	47 (95.9%)
<i>Radiotherapy, n (%)</i>	50 (100%)
<i>Dose Level in Gray, n (%)</i>	
70 Gy	36 (75%)
66 Gy	2 (4,2%)
50 Gy	1 (2,1%)
39 Gy	8 (16,6%)
30 Gy	1 (2,1%)
<i>Follow-up Duration (months), median (IQR)</i>	20 [15.5 – 24.6]
<i>Deaths, n (%)</i>	20 (40%)
<i>2-Year Overall Survival, n (%)</i>	14 (25%)

With a median follow-up of 20 months, 22 patients (44%) had deceased with a median time to death of 12 months. Fourteen patients (28%) were alive, and 14 patients (28%) were lost to follow-up. The 2-year overall survival rate was estimated at 25% (Figure 1).

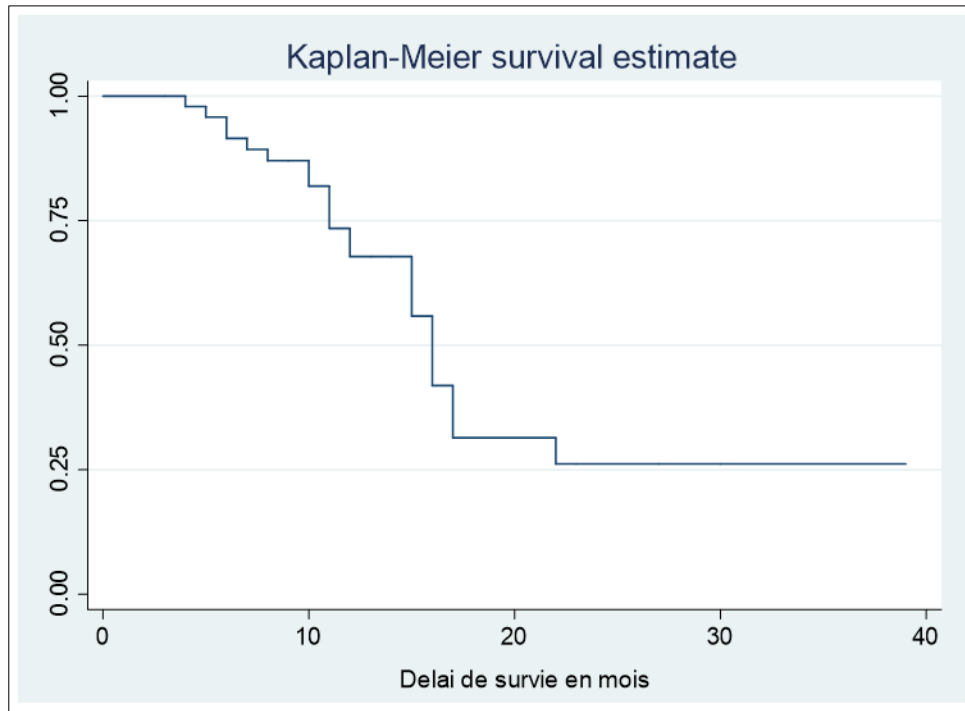


Figure 1 Survival of patients with hypopharyngeal carcinoma receiving a definite chemoradiotherapy (n=50)

In multivariate statistical analysis, it was found that the presence of feeding gastrostomy (p=0.044), administration of induction chemotherapy (p=0.012), and radiotherapy dose less than 70 Gy (p=0.020) were associated with poorer outcomes.

Table 4 Summary of the analysis and factor of poorer outcomes

Palliative car		Issue						Total	P value
		Deceased		Living		lost to follow-up			
		n	%	n	%	n	%		
Tracheostomy Tube	No	8	23.53	13	38.24	13	38.24	34	0.063
	Yes	6	37.50	9	56.25	1	6.25	16	
Nasogastric Tube	No	13	29.53	17	38.64	14	31.82	44	0.099
	Yes	1	16.67	5	83.33	0	0.00	6	
Feeding Gastrostomy	Yes	1	16.67	5	83.33	0	0.00	6	0.044*
	No	8	26.67	10	33.33	12	40.00	30	
	Yes	6	30.00	12	60.00	2	10.00	20	

Table 5 Evolution according to radiotherapy dose

Evolution	Radiotherapy Dose					
	Minimum	Average	SD	Médian	Mode	Maximum
Living	39	66	11.2	70	70	70
Deceased	30	56	15.8	70	70	70
lost to follow-up	66	69	1.4	70	70	70

Table 6 Evolution according to treatment protocol

Radiotherapy Treatment	Evolution				Lost to Follow-Up		Total	P value
	Living		Deceased		N	%		
	N	%	N	%	N	%		
Neoadjuvant Chemotherapy followed by Chemoradiotherapy	3	11.54	13	50.00	10	38.46	26	0.012
Chemoradiotherapy	6	66.67	2	22.22	1	11.11	9	
Exclusive Radiotherapy	1	100.0	0	0.00	0	0.00	1	

4. Discussion

Hypopharyngeal carcinoma, though rare, carries a poor prognosis due to late diagnosis and high metastatic potential [1]. The incidence is higher in Asia, with Africa ranking third in terms of mortality [2]. In Senegal, hypopharyngeal tumors rank highest among upper aerodigestive tract cancers [3][5]. However, these are hospital series, and estimating the incidence at a national scale is challenging due to the absence of a functional cancer registry. In Western literature, the average age of onset for hypopharyngeal carcinoma is around 55 years for men and 60 years for women [1]. Studies conducted in Senegal show a younger average age of 45.8 years. This difference in mean age averages could be attributed to population age disparities between Western and African countries. Globally, hypopharyngeal cancer incidence is five times higher in men than in women [6]. However, there is increasing evidence of rising and even a predominance of female cases [4][7][8].

This emerging trend suggests changes in smoking and alcohol consumption behaviors, two well-established risk factors. In our cohort, women accounted for 64% of cases, consistent with findings from previous Senegalese studies [4][7].

Major risk factors include smoking, alcohol consumption, occupational exposures, and possibly human papillomavirus (HPV) infection, which in combination with iron deficiency anemia may explain the increased incidence of this condition in young females. In our study, 64% of patients were women, and the age group 30-40 represented 22% of the cohort [9][10][11]. Initiatives aimed at improving oral hygiene and recognizing genetic factors also appear to play a role in prevention [12].

However, it is noteworthy that smoking and alcohol consumption, known risk factors for hypopharyngeal cancer, are not prevalent in our cohort. Indeed, the majority of studies have found a low frequency of smokers [15][4]. This low smoking rate may be explained by sociocultural and religious habits. In our regions, other yet unidentified risk factors, including chronic iron deficiency anemia prevalent among women due to poor dietary iron intake, heavy menstruation, and multiple pregnancies; diets rich in smoked and salted foods; as well as prolonged exposure to domestic smoke, warrant further prospective investigation in our context.

Upper aerodigestive tract cancers related to HPV predominate in North America and Europe, with high absolute frequencies [13]. In sub-Saharan Africa, HPV prevalence is low, and few studies have explored its role in hypopharyngeal cancers, estimating it at 13

%. [14] No patients in our study were tested for HPV, although its involvement is suspected due to the young age of patients. Systematic investigation of HPV infection in hypopharynx biopsies is necessary to explore risk factors in our context.

These tumors, often detected at an advanced stage, typically present with dysphagia as the main symptom [9]. In our series, dysphagia was found in 92% of cases, becoming completely obstructive in 40% necessitating digestive diversion and in 32% requiring tracheostomy.

The delay in seeking medical consultation is an aspect not studied extensively in Western series. In our series and local hospital data, this delay was 6 months [3][19]. This prolonged delay may be attributed to a shortage of specialists, specialized treatment centers, and inadequate health education [19]. Late consultation may also explain advanced stages at diagnosis.

Historically, radical surgery was the standard treatment, but conservative approaches, particularly chemoradiotherapy, have become more common indications [10][11][12]. None of our patients underwent radical surgery; however, it remains indicated for resectable advanced stages and salvage after failure of concurrent chemoradiotherapy protocols.

Neoadjuvant chemotherapy for locally advanced forms is not a standard practice; it is reserved for patients with rapidly progressive disease or N3 [15]. In our cohort, this neoadjuvant chemotherapy is associated with poorer survival with a p-value of 0.012, as it delays concurrent chemoradiotherapy with its associated toxicities, resistance, and cellular repopulation. Hence, upfront concurrent chemoradiotherapy should be favored. However, it is important to note that the chemotherapy agents used in our cohort differ from those described in other studies due to logistical and financial constraints [23].

The importance of supportive care, especially enteral nutrition, is crucial for successful treatment outcomes [16][17], even though in our study, the placement of gastrostomy feeding tubes was associated with poorer survival with a p-value of 0.044. This result raises questions about the timing and utilization of gastrostomy tubes, particularly with the involvement of a nutritionist, necessitating further research to optimize outcomes.

All our patients were treated with three-dimensional conformal radiotherapy (3D-CRT) due to the unavailability of intensity-modulated radiotherapy (IMRT), which is the standard treatment for this site. It was found that a radiotherapy duration exceeding 45 days ($p=0.044$) and lower dose levels below 70 Gy ($p=0.020$) negatively influence patient prognosis.

Despite advancements in treatments, the 2-year overall survival rate in our study was 25%, which, although improved compared to earlier data, still represents a poor prognosis [5][4].

The limitations of this study are mainly associated with its retrospective nature, which introduces biases, and issues with post-therapeutic follow-up, particularly for patients in the sub-region.

5. Conclusion

Despite advances in the management of hypopharyngeal cancer, the prognosis remains grim. Persistent challenges include contextualized specific risk factors, early diagnosis, care coordination, and enteral nutrition. A multidisciplinary approach and improved patient follow-up organization are essential to enhance long-term outcomes.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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