

## Retrospective Study

# Hypopharyngeal cancer trends in a high-incidence region: A retrospective tertiary single center study

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## Abstract

### BACKGROUND

Hypopharyngeal cancer has the bleakest prognosis among head and neck cancers due to its extensive submucosal involvement, advanced tumor stage, and limited surgical reconstruction options. Its primary causes include alcohol consumption, tobacco use, genetic predisposition, 1<sup>st</sup> diet, and socioeconomic conditions. While

squamous cell carcinoma (SCC) accounts for 95% of hypopharyngeal tumors, it remains a rare form, comprising only 3%-5% of all SCC cases in the head and neck region. Globally, Central and Eastern Europe have the highest incidence rates for males (3.9 per 100000) and the third highest for females (2.26 per 100000), underscoring the significance of this seemingly uncommon condition. In Romania, hypopharyngeal cancer ranked 24<sup>th</sup> in incidence rate, with 634 new cases in 2020.

### AIM

To study the incidence, treatment and survival rates of hypopharyngeal tumor cases in a major ear, nose, throat (ENT) surgical center.

### METHODS

A retrospective epidemiological clinical study was conducted on patients diagnosed and treated for hypopharyngeal cancer at the ENT department of "Carol Davila Central University Emergency Military Hospital" in Bucharest between January 2018 and August 2022. The study included 53 patients and was authorized by the Ethics Committee of Titu Maiorescu Doctoral School (Bucharest, Romania) and the Ethics Committee of Carol Davila Central University Emergency Military Hospital (Bucharest, Romania). Inclusion criteria required a positive histopathological diagnosis of hypopharyngeal cancer, tumor localization in the hypopharyngeal region, and informed consent for data usage. Exclusion criteria involved major psychiatric pathologies and disagreement for data usage. Diagnosis was based on ENT assessment, imaging reports, and laboratory data. Treatment methods were determined based on various factors. Additional tools, such as Adult Comorbidity Evaluation-27 and Karnofski Performance Status Scale, were used for risk assessment and functional capacity evaluation. Quality of life aspects were measured using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Head and Neck-35 questionnaire.

### RESULTS

Our retrospective study examined 53 patients with hypopharyngeal cancer between January 2018 and August 2022. The majority of patients were male (94.3%), with an average age at diagnosis of 62.5 years. Among the patients, 20.75% were employed, 66.03% were retired, and 9.43% were unemployed. Smoking was prevalent among 69.81% of patients, while alcohol consumption was frequent in 32.07% of cases. The tumors were mostly diagnosed at an advanced stage (stage IV) and were predominantly SCC. Comorbidities were present in 83.01% of patients, with cardiovascular diseases being the most common. Dysphagia and neck mass were the most common symptoms reported. Treatment methods included surgery, radiation therapy, and chemotherapy. A favorable treatment response was observed in 22.64% of cases, while relapse occurred in 6 cases. Follow-up data was unavailable for some patients.

### CONCLUSION

In summary, our findings align with existing literature; however, we observed a higher severity.

**Key Words:** Hypopharyngeal; Cancer; Organ conservation therapy; Chemotherapy; Radiotherapy; Surgery

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**Core Tip:** This retrospective study analyzed 53 hypopharyngeal cancer patients' data, focusing on diagnostic methods, treatment strategies, and quality-of-life assessments using Adult Comorbidity Evaluation-27, Karnofski Performance Status Scale, and European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Head and Neck-35. Our findings discovered that most patients had advanced stage cancer, frequent smoking history, and comorbidities. Various treatments were applied, with mixed responses and a 30.18% follow-up rate. Late-stage diagnosis resulted in decreased capacity function; 83% had comorbidities. Organ conservation therapies were preferred by 43.39%, driven by similar survival rates and quality of life considerations. In conclusion, all the data we found was similar to the one found in literature, but with a higher degree of severity and a younger age at diagnosis compared to the most studies.

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## INTRODUCTION

Hypopharyngeal cancer is one of the most challenging pathologies in the head and neck region, due to the aggress-

iveness, late detection and advanced stages at diagnosis. With a rich submucosal extent, no specific or early symptoms and with a low survival rate, advanced stages on diagnosis and the silence of the regional symptoms, this pathology goes undetected for a long period of time, and usually is found by accident in early stages. In most cases, the symptoms that bring the patient to the hospital are the ones from the surrounding regions (laryngeal and cervical esophagus involvement)[1,2].

Globocan statistics shown that in 2020 the number of new cases of hypopharyngeal cancer for both sexes was 84254 and the number of deaths was 38599, worldwide. In Central and Eastern Europe, the region with the highest incidence rate for males (3.9 per 100000) and the third incidence rate for females (2.26 per 100000), out of 9145 of new cases diagnosed in 2020, 8413 were males and 732 females. The death number reached to 5255 for both sexes: 4831 males and 424 females. In Romania, the hypopharyngeal cancer is ranked on the 24<sup>th</sup> place based on its incidence rate, with 634 new cases, 441 deaths (23<sup>rd</sup> place) and a 5-year prevalence of 1108 cases[3].

In the literature described another general aspect of this disease, found all around the globe that hypopharyngeal cancer usually affects patients with low socio-economic status, with a positive history of alcohol and tobacco abuse, factors that also lead to diagnosis delays, usually when the disease is advanced, their quality of life is severely impaired and their survival might be affected. The hypothesis available today on alcohol mechanisms that lead to carcinogenesis are: Alcohol is a direct carcinogen to the cells, alcohol acts as a carcinogenic promotor of smoking, or both variants[4]. Others factors that were proven to be involved in the hypopharyngeal cancer development are: Presence of infection with human papilloma virus[4,5], an controversy factor, that other studies missed to show a connection to cancer survival or hypopharyngeal cancer development, limited only to the oropharyngeal region[6-9]. Other proven risk factors that predispose to hypopharyngeal cancer are: From a genetic predisposition (Plummer-Vinson, also known as Paterson-Brown-Kelly syndrome[4], in the Japanese population, Yamashita *et al*[10] found genetic predisposition on patients with alcohol dehydrogenase 1B10, aldehyde dehydrogenase 2 as additional factors to smoking cigarettes and alcohol consumption), environmental related factors (long term exposure to asbesto[8], formaldehyde and coal dust[11]).

Hypopharyngeal cancer associates in 40% of cases lymph node metastases, and when first seen, 50% of patients present with advanced stages T3 N1-2[12]; also associates a high rate of mortality, (in Europe the rate is up to 30% in the first year of diagnosis and the 5-year survival 25%)[1]. Because early symptoms such as swallowing difficulties and presence of lateral cervical mass are usually neglected, the detection in early stages is rare and more commonly, the clinical features that bring the patient are: Hoarseness and dyspnea, dysphagia and referred otalgia, symptoms that usually indicate an extended tumor to the larynx, paralyzed recurrent laryngeal nerve or involvement of the posterior pharyngeal wall and prevertebral fascia[1,12].

Hypopharyngeal cancer treatment was based up to the 1980 on standard radical surgical excision associated postoperative with radiation therapy or radiotherapy alone. Conservative procedures begun to be used when the laryngeal conservation procedures were developed in 1960. Nowadays even if there is a lack of standard treatment for this type of pathology, the most frequent used methods remain primary radiochemotherapy and others continue to use the primary surgical technique followed by adjuvant radiotherapy[1]. Because it is a rare pathology usually found in late stages, the treatment options are limited and consist in surgical excision of larynx and partial or complete resection of the pharynx, followed by radiation therapy and organ conservation procedures which aim to keep the larynx and pharynx-radiation therapy and chemotherapy, either simultaneously (concurrent chemoradiation therapy) or induction therapy followed by radiation therapy in case of treatment response and in case of failure, surgical excision. The main issue in the treatment methods available today is that none of them associates significant improved survival.

## MATERIALS AND METHODS

A descriptive, observational, nonrandomized retrospective epidemiological clinical study was conducted on data retrieved from patients diagnosed and treated for hypopharyngeal cancer between January 2018 and August 2022 in the ear, nose, throat (ENT) department of "Carol Davila Central University Emergency Military Hospital" in Bucharest. In this period, 53 patients were diagnosed with hypopharyngeal cancer. This study was authorized by the Ethics Committee of Titu Maiorescu Doctoral School (Bucharest, Romania) number 15/2022 and by the Ethics Committee of Carol Davila Central University Emergency Military Hospital (Bucharest, Romania) number 538/2022. All patients provided written informed consent for data usage and publication in research purposes.

Inclusion criteria accounted for inclusion on the study were: Positive diagnosis confirmed by histopathological report, localization of the tumor in the hypopharyngeal region, absence of major psychiatric pathologies, the presence of the informed consent and agreement of usage for personal data in research purposes. Exclusion criteria consisted of the presence of major psychiatric pathologies, other cancers located in the laryngeal or oropharyngeal region without involvement of the hypopharynx, patients that did not agree for usage of personal data for research purposes.

Diagnosis was based on ENT assessment completed with flexible nasopharyngoscopy or rigid endoscopy with variable grades (0°, 30°, 70°, 90°); esophagogastroduodenoscopy in order to evaluate the extension of the tumor; imagistic reports lead to carcinogenesis are computed tomography (CT) and contrast magnetic resonance imaging (MRI) were used for tumor staging and, for a few patients, even Positron Emission Tomography-CT was necessary to assess the residual disease. Laboratory data included: Complete blood count, coagulation profile (International Normalized Ratio, Prothrombil Time Test), erythrocyte sedimentation rate, glucose, urea, and creatinine levels, bilirubin, serum alanine aminotransferase, serum aspartate aminotransferase, sodium, potassium, serum amylase and C-reactive protein. All the patients underwent direct laryngoscopy with biopsy with general anesthesia and positive diagnosis was made through histopathological report.

The treatment methods used in clinic were chosen considering age, tumor parameters [histological type, location, tumor, node, metastasis (TNM) and American Joint Committee on Cancer (AJCC) classification], general status-comorbidities, personal history of cancer, expected result and personal preference. Optimal treatment strategies were discussed by our oncological board according to the Romanian nation-wide head and neck cancer protocols which considered all the factors mentioned above.

Additionally, Adult Comorbidity Evaluation-27 (ACE-27) was used in order to objectively measure and assess the risk of developing acute severe toxicities for patients that underwent chemoradiation therapy and as a prognostic tool of mortality and complications for patients that were surgically treated[6,7]. Karnofski Performance Status Scale was completed based on the initial visit and used in order to grade the functional capacity[8]. The quality-of-life (QoL) aspects were measured based on the questionnaire developed by the European Organisation for Research and Treatment of Cancer using the module for head and neck cancer, Romanian version. Considering that the study is retrospective and the questionnaire cannot be applied to some of the patients, we evaluated the main items (pain, swallowing, opening mouth, senses, speech, social contact and eating, pain killers) based on the information obtained from the data charts and adding the presence or absence of the acute respiratory distress syndrome on visit.

## RESULTS

Based on the inclusion/exclusion criteria used, 53 patients diagnosed with hypopharyngeal cancer were admitted in the ENT department between January 2018 and August 2022. The sex ratio was 50:3 (94.3% males, 5.66% females). In this group, a percent of 20.75% (11 patients) were employed, 66.03% (35 patients) were retired and 9.43% (5 patients) were not employed. This proportion is partially confirmed by a more advanced age at diagnosis for a majority of patients. The average age at diagnosis was 62.5 years old, with the youngest patient being 45 years and the oldest at 81 years.

As by Romanian government-controlled supervision board that defines and regulates working conditions and their potential hazardous impact, only 9 patients (16.98%) were registered as working in a hazardous environment, 56.6% (30 patients) there was a safe workplace and for 24.52% (13 patients) information regarding this aspect was not disclosed by the employer.

Regarding behavioral patterns we identified smoking for 69.81% (37 patients), 24.52% (13 patients) quit smoking for more than a year, but have had a history of smoking for more than a decade and only 3.77% (2 patients) were nonsmokers. Non-smoking patients had a certified toxic environment at their workplace with long-term exposure and fall into the category of chronic alcohol consumption. Alcohol consumption use was described as frequent (daily or more than twice a week) for 32.07% (17 cases); occasionally (once a week or less often) for 64.1% and 5.66% (3 patients) denied this habit.

The overall anatomic location of the tumors in our study is displayed in [Table 1](#), while the tumor histological pattern are represented in [Table 2](#).

Histopathological investigation showed squamous cell carcinoma (SCC), with various subtypes ([Table 3](#)) and gradings ([Table 4](#)). An aspect that we find important to emphasize is the lack of early detected cases (T1-2), with 48 cases out of 53 diagnosed in stage IV. In our study group, the grading with the highest incidence (16 patients out of 53) was G2, followed by G3 (12 patients), G1 (3 patients) and G4 (1 patient). For 21 patients, the grading was not specified ([Table 5](#)).

As this is a small group-based study on a rare pathology, we cannot correctly estimate the survival rate of patients (Hazard Ratio) between gradings.

TNM and AJCC cancer staging is shown in [Table 4](#), with all the cases in advanced forms upon diagnosis (Stage III and IV) and absence of early stages. Cervical lymphadenopathy was present on diagnosis for 52 out of 53 patients (98.1%) ([Table 6](#)).

The presence of comorbidities was evaluated using ACE-27[6] with 83.01% (44 patients) having various types of concurrent pathologies, the most frequent affected systems: Cardiovascular (69.81%); endocrine system/diabetes mellitus (28.30%); respiratory (22.64%); and malignancy (16.98%). In [Table 5](#) we have described in detail our findings. Most patients presented with moderate decompensation (43.39%, 23 cases) and mild decompensation (18.86%, 10 cases); 13.20% (7 patients) had severe decompensations; 9.43% (5 cases) had no decompensation and for 15.08% (8 cases) it was unknown ([Table 7](#)).

Even though many of the tumors encountered were clinically evident, we also made use of imaging reports (CT, MRI with contrast agents) to sort our differential diagnosis or to evaluate the extent of the preexistent ailments such as tuberculosis[9] or other benign tumors[10].

Karnofski Performance Status Scale was used to better assess the patients on the functional capacity of patients on their first visit. We found that the majority of patients needed assistance (functional capacity of 50%-60%), confirming the fact that most of the cases were diagnosed in advanced stages, when complications arise. [Table 8](#) shows the patients capacity on diagnosis.

At presentation, the most frequent symptoms accused by the patients were dysphagia (92, 45%) and neck mass (90, 56%) and the least frequent being headache and hemoptysis (2 cases, 3.77%) ([Table 9](#)).

Treatment methods included surgical approach (total laryngectomy and partial pharyngectomy) in 6 patients (11.32%) followed by radiation therapy, among them, 2 patients (3.77%) needed chemotherapy for relapses; 23 patients (43.39%) were treated with organ-conservation therapies (radiation therapy and chemotherapy); 4 patients (7.54%) made tracheostomy procedure and were expected to begin the organ conservation therapy after discharge; 1 patient (1.88%) received chemotherapy and 16 patients (30.18%) could not be evaluated due to the lack of follow-up visits.

**Table 1 Squamous cell carcinoma of the oral cavity, larynx, oropharynx and hypopharynx, as stated by European Head and Neck Society-European Society for Medical Oncology-European Society of Radiotherapy & Oncology Clinical Practice guidelines for diagnosis, treatment and follow-up-management of hypopharyngeal cancer (Stage I-IV B)**

TNM Stage	Standard	Option
cT1-2 cN0 cM0	RT  Conservation larynx surgery (T and N), followed by RT and CRT if indicated	
cT1-2 cN1-3 M0; cT3 cN0-3 M0	Concomitant CRT  If laryngectomy necessary, concomitant CRT (T and N), or induction ChT followed by RT (T and N) in case of complete or partial response after induction or surgery in case of stable or progressive disease after induction	Surgery followed by RT or CRT if indicated
cT4a cN0-3 cM0	Surgery (T and N), followed by RT or CRT if indicated	CRT  Induction ChT followed by RT (T and N) in case of complete or partial response after induction or surgery (T and N) in case of stable or progressive disease after induction
cT4b cN0-3 cM0		Induction ChT followed by RT for responders (T and N)  Concomitant CRT  Palliative treatment: systemic ChT/ immunotherapy and/or palliative RT and/or BSC

BSC: Best supportive care; ChT: Chemotherapy; CRT: Chemoradiotherapy; M: Metastasis; N: Node; RT: Radiotherapy; T: Tumor; TNM: Tumor, node, metastasis.

**Table 2 Location patterns of primary tumor**

Hypopharynx	Hypopharynx and larynx	Oro-hypopharynx	PEJ	Hypopharynx + larynx + esophageal inlet
11 cases	33 cases	2 cases	6 cases	1 case
20.75%	62.26%	3.77%	11.32%	1.88%

PEJ: Pharyngoesophageal junction.

**Table 3 Histopathological subtypes of tumor**

Histopathologic subtype	Case number	Percentage
Keratinized	36	67.9%
Non keratinized	6	11.32%
Spindle cell	4	7.54%
Not specified	7	13.2%

Evolution after treatment was deemed as “Favorable” (complete response at treatment, absence of tumor findings in ENT examination and imagistic reports) for 22.64% (12 patients); “Not favorable” (the primary tumor did not respond to the treatment used, tumoral growth or early relapse before treatment completion) for 24.52% (13 patients) and “Stationary” (the tumor size was not modified by the treatment; patients with significant post-radiation edema that made impossible the treatment response evaluation) for 22.64% (12 patients). This group is the only one in which we expect alterations in time, because we included the need for a closer follow-up for estimating the final response to treatment. A total of 16 cases (30.18%) included patients with no follow ups for whom we do not have additional clinical information.

We encountered 6 cases of cancer relapse after completion of the treatment (2 cases after surgical treatment and radiation therapy and 4 cases after chemoradiation therapy), 10 cases could not be followed up and we have not additional data regarding tumor relapse.

**Table 4 Grading aspects of the primary tumor**

Tumor grading	Case number	Percentage
Grade 1	0	0%
Grade 2	16	30.1%
Grade 3	12	22.64%
Grade 4	1	1.88%
Unspecified	21	39.62%

**Table 5 Histopathological investigation of the study showing squamous cell carcinoma, with various subtypes**

			Tracheotomy			Total
			Elective	Without	Emergency	
Grading	G1	Frequency			3	3
		Percentage of same grading			100.0%	100.0%
		Percentage of tracheotomies			12.0%	5.7%
	G2	Frequency	4	4	8	16
		Percentage of same grading	25.0%	25.0%	50.0%	100.0%
		Percentage of tracheotomies	36.4%	23.5%	32.0%	30.2%
	G3	Frequency		7	5	12
		Percentage of same grading		58.3%	41.7%	100.0%
		Percentage of tracheotomies		41.2%	20.0%	22.6%
G4	Frequency			1	1	
	Percentage of same grading			100.0%	100.0%	
	Percentage of tracheotomies			4.0%	1.9%	
N	Frequency	7	6	8	21	
	Percentage of same grading	33.3%	28.6%	38.1%	100.0%	
	Percentage of tracheotomies	63.6%	35.3%	32.0%	39.6%	
Total	Frequency	11	17	25	53	
	Percentage of same grading	20.8%	32.1%	47.2%	100.0%	
	Percentage of tracheotomies	100.0%	100.0%	100.0%	100.0%	

## DISCUSSION

This study aimed to search if the epidemiology of hypopharyngeal cancer was different in a high-incidence region than literature reviews. The first important aspect was that all the patients from our study were diagnosed in advanced stages (Stage IV A: 56.60%; Stage IV B: 26.41%; Stage III: 9.43%; Stage IV C: 7.54%), unlike literature review in which we consistently found a small percentage of patients early diagnosed[11-13]. The average age at diagnosis was 62.5 years old, a few years younger than some literature reports[1,12,14-16] and older than other studies[17,18], but maintaining a close age to the one reported in previous studies.

The majority of patients had a low economic status (86.78% unemployed, retired or disabled), confirming previously done studies[19-21]. Social behavior confirmed for 94.33% of patients chronic smoking, for 32.07% patients frequent alcohol intake[22-26]. Occupational exposure to hazardous environment was encountered in 16.98% of patients[27-30].

The most frequent symptom accused was dysphagia (92.45%), followed by neck mass (90.56%) and hoarseness (75.4%), symptoms usually described by late-stage diagnosed patients[1,12,31]. All the patients described the manifestation of more than one symptom. Histopathology reports showed only variants of SCC with more than half (54.62%) graded as 2, 3 and 4.

Another aspect of late-stage diagnosis was confirmed by decreased capacity function for a large group of patients shown by the Karnofski Performance Status Scale (more than 70% of patients graded with 60% capacity or less) and from the ACE-27 we found a high rate of patients with present comorbidities (83%) in which more than half have had moderate or severe decompensations.

**Table 6 American Joint Committee on Cancer and tumor, node, metastasis staging of the cases**

AJCC stage	TNM stage	Cases	Percentage
Stage 0	Tis N0 M0	0	0
Stage I	T1 N0 M0	0	0
Stage II	T2 N0 M0	0	0
Stage III	T3 N3 M0; T1-3 N1 M0	5	9.43%
Stage IV A	T4a N0/1 M0; T1-4a N2 M0	30	56.60%
Stage IV B	T4b any N M0; any T N3 M0	14	26.41%
Stage IV C	Any T any N M1	4	7.54%

AJCC: American Joint Committee on Cancer; TNM: Tumor, node, metastasis.

**Table 7 Adult Comorbidity Evaluation-27 comorbidities in hypopharyngeal cancer patients**

Comorbidities (system affected)	Patients	Percentage	Total
Cardiovascular	37	69.81%	44 cases (83.01%)
Pulmonary	12	22.64%	
Diabetes mellitus	15	28.30%	
Malignancy (other than the present illness)	9	16.98%	
Allergies	1	1.88%	
Other comorbidities (gastrointestinal, substance abuse, renal, etc.)	25	47.16%	

**Table 8 Karnofski Performance Status Scale definitions rating**

KPSs grade	Functional capacity level	Patients	Percentage
100%	Normal, no complaints, no evidence of disease	0	0%
90%	Able to carry on normal activity. minor signs or symptoms of disease	1	1.88%
80%	Normal activity with effort; some signs or symptoms of disease	8	15.09%
70%	Cares for self; unable to carry on normal activity or to do active work	6	11.32%
60%	Requires occasional assistance. but is able to care for most of his personal needs	21	39.62%
50%	Requires considerable assistance and frequent medical care	11	20.75%
40%	Disabled; requires special care and assistance	4	7.54%
30%	Severely disabled; hospital admission is indicated although death is not imminent	2	3.77%
20%	Very sick: Hospital admission necessary; active supportive treatment necessary	0	0%
10%	Moribund; fatal process progressing rapidly	0	0%
0%	Dead	0	0%

KPSs: Karnofsky performance scores.

Treatment options in our study were broad, but we have seen a trend of preference for organ conservation therapies for 43.39% of patients[14,15,20,32], partially explained by the similar survival rates of both methods[33,34]. Organ conservation therapies gained ground as the primary treatment option since 1990[14]. These therapies are applied to all stages, including advanced ones and are frequently elected as main treatment from the QoL perspective[35-40]. However, organ preservation-oriented strategies do not always correlate with the function preservation goal[40-45].

One of the most important drawbacks of our study consisted of follow-up evaluations, with a high number of patients that did not respect the future appointments (30.18%). Second, the impact of the coronavirus disease 19 (COVID-19) pandemic and the restrictions applied during the year 2020 made it difficult for the patients to receive any form of healthcare, except the emergency situations on the public hospitals. Because we have stated earlier that hypopharyngeal

**Table 9 Presenting symptoms**

Symptom	Frequency	Number of patients
Dysphagia	92.45%	49
Neck mass	90.56%	48
Hoarseness	75.4%	40
Shortness of breath	67.9%	36
Weight loss	52.83%	28
Otalgia	15.09%	8
Hemoptysis	3.77%	2
Headache	3.77%	2

The columns do not total 100% because patients presented more than one symptom at once.

cancer patients usually have a lower social status we can suppose that they primary address the public health system.

In the surgically treated group, no major postoperative complications were recorded, such as septic shock[46] that sometimes, might occur after radical excision of such tumors, especially those located in the aerodigestive tract. The only complication we recorded on the surgically treated branch was pharyngocutaneous fistula after infection, treated with antibiotics according the antibiogram and surgical closure of the defect[47-49].

Considering the fact that in this study the average age of patients upon diagnosis was 62.5 years old, that 50 patients out of 53 were smokers or with a long history of smoking (more than 10 years), with affirmative habitual drinking and 44 out of 53 patients presented with moderate and severe decompensation of concurrent pathologies, we highlight the necessity of a screening plan for the public health system in order to improve early diagnosis such as for patients that present in a hospital setting, if they are aged over 60 years old, with positive alcohol and tobacco history it would be helpful to include an ENT exam when, which is a noninvasive procedure but can be useful in detection of early staged disease alterations. The main limit of the present study is the low number of patients and the fact that due to the coronavirus pandemic the public health system was limited, so the patients had a restrictive access to health care.

## CONCLUSION

Hypopharyngeal cancer patients in the high-incidence region of this study were predominantly diagnosed at advanced stages, unlike the findings in literature where a small percentage of early-stage cases were observed[1,4]. The average age at diagnosis in this study was 62.5 years, which was slightly younger compared to some literature reports but consistent with previous studies[1,4]. The majority of patients had a low economic status, as they were unemployed, retired, or disabled, supporting findings from previous studies. Social behaviors such as chronic smoking, frequent alcohol intake, and occupational exposure to hazardous environments were prevalent among the patients, aligning with previous research. Dysphagia, neck mass, and hoarseness were the most commonly reported symptoms, which are often associated with late-stage diagnosis. Histopathology reports indicated that all cases were variants of SCC, with more than half graded as moderate to severe. Functional capacity, as assessed by the Karnofsky Performance Status Scale, was significantly reduced in a large proportion of patients, reflecting late-stage diagnosis and disease progression. The presence of comorbidities was high among the patients, with a significant number experiencing moderate or severe decompensations. Organ conservation therapies were preferred treatment options, likely influenced by similar survival rates compared to radical surgical approaches and considerations for quality of life. Challenges in follow-up evaluations were noted, with a substantial number of patients missing their appointments, potentially affected by the COVID-19 pandemic and limited access to healthcare. In the surgically treated group, no major complications were recorded, but a pharyngocutaneous fistula was observed, which was successfully managed with antibiotics and surgical closure. Considering the demographic characteristics and habits of the patients, it is crucial to develop a screening plan within the public health system to improve early detection of hypopharyngeal cancer, especially for older individuals with a history of alcohol and tobacco use.

## ARTICLE HIGHLIGHTS

### Research background

Hypopharyngeal cancer, characterized by extensive submucosal involvement, advanced tumor stage, and limited surgical reconstruction options, has the poorest prognosis among head and neck cancers. Its primary causes include alcohol consumption, tobacco use, genetic predisposition, diet, and socioeconomic conditions. Although squamous cell

carcinoma (SCC) comprises the majority of hypopharyngeal tumors, it remains a rare form, representing only 3%-5% of all SCC cases in the head and neck region. The high incidence rates in Central and Eastern Europe, with Romania ranking 24<sup>th</sup> in incidence rate and reporting 634 new cases in 2020, emphasize the importance of understanding this seemingly uncommon condition.

### **Research motivation**

The motivation of the present study was to conduct a descriptive, observational, nonrandomized retrospective epidemiological clinical study on patients diagnosed and treated for hypopharyngeal cancer, to assess various factors such as diagnosis methods, treatment approaches, laboratory data, comorbidity evaluation, performance status, and quality-of-life (QoL) aspects. The study's motivation includes the need to understand the epidemiology and clinical characteristics of hypopharyngeal cancer in the given population and contribute to the existing knowledge in this field.

### **Research objectives**

Our objectives were to assess epidemiological characteristics of hypopharyngeal cancer by analyzing demographic and clinical data, to evaluate diagnostic methods, including ear, nose, throat (ENT) assessments and various imaging techniques. Investigate treatment approaches aligned with national guidelines, to evaluate the risk of toxicities in chemoradiation therapy and prognostic value of Adult Comorbidity Evaluation-27 (ACE-27) scale, to evaluate functional capacity and quality of life using Karnofsky Performance Status Scale and the European Organisation for Research and Treatment of Cancer (EORTC) using the module for head and neck cancer (QLQ-H&N35) questionnaire and to identify limitations and challenges in the retrospective study design, considering socioeconomic factors and the impact of the coronavirus disease 19 (COVID-19) pandemic on healthcare access.

### **Research methods**

This retrospective epidemiological clinical study analyzed data from 53 patients diagnosed and treated for hypopharyngeal cancer between January 2018 and August 2022 in an ENT department of a major clinical surgical center. Inclusion criteria required positive histopathological diagnosis, hypopharyngeal tumor localization, absence of major psychiatric pathologies, and informed consent. Diagnostic methods included ENT assessment, flexible/rigid endoscopy, esophagogastroduodenoscopy, imaging techniques [computed tomography (CT), magnetic resonance imaging, Positron Emission Tomography-CT], and laboratory tests. Treatment decisions were based on age, tumor parameters, general status, and national guidelines. ACE-27, Karnofski Performance Status Scale, and EORTC QLQ-H&N35 were used to assess toxicity risk, functional capacity, and quality of life respectively.

### **Research results**

In this study, 53 patients with hypopharyngeal cancer were included based on the predefined criteria. The majority of patients were male (94.3%), and the average age at diagnosis was 62.5 years. Smoking was prevalent among 69.81% of patients, while alcohol consumption was reported in 32.07% of cases. The tumors were predominantly SCC, with most cases diagnosed at an advanced stage. Comorbidities were present in 83.01% of patients, with cardiovascular diseases being the most common. Imaging reports were used for differential diagnosis and evaluating disease extent. Karnofsky Performance Status Scale indicated that the majority of patients had reduced functional capacity at the time of diagnosis. Dysphagia and neck mass were the most frequent symptoms reported. Treatment approaches varied, including surgery, radiation therapy, chemotherapy, and organ-conservation therapies. The treatment response was favorable in 22.64% of cases, while relapse occurred in 6 patients. A proportion of patients lacked follow-up data.

### **Research conclusions**

Hypopharyngeal cancer patients in this high-incidence region were predominantly diagnosed at advanced stages, unlike previous studies reporting a small percentage of early-stage cases. The average age at diagnosis was 62.5 years, consistent with previous research. The majority of patients had a low economic status, with unemployment, retirement, or disability status. Prevalent social behaviors included chronic smoking, frequent alcohol intake, and occupational exposure to hazards. Common symptoms reported were dysphagia, neck mass, and hoarseness, indicative of late-stage diagnosis. Histopathology revealed SCC variants, mostly graded as moderate to severe. Reduced functional capacity was observed in many patients, reflecting late-stage diagnosis and disease progression. Comorbidities were common, with moderate to severe decompensations. Organ conservation therapies were favored, considering similar survival rates to radical surgery and QoL considerations. Challenges in follow-up evaluations were noted, potentially influenced by the COVID-19 pandemic. In the surgically treated group, no major complications occurred, except for a successfully managed pharyngocutaneous fistula.

### **Research perspectives**

Perspectives for further research include an improved follow-up rates as future research should focus on understanding the reasons behind the high number of missed follow-up appointments in hypopharyngeal cancer patients. Investigating barriers to follow-up, such as socioeconomic factors, patient education, and healthcare system accessibility, can provide insights into strategies to improve compliance and ensure continuity of care. Also, the impact of the COVID-19 pandemic, now greatly diminished, should allow us to examine the long-term consequences of delayed or interrupted care for hypopharyngeal cancer patients. Understanding the impact of the pandemic on diagnosis, treatment, and outcomes can inform future strategies for managing cancer care during similar crises. Further research should investigate healthcare disparities and access barriers for this population, including factors such as socioeconomic status, health insurance

coverage, and geographic location. Identifying and addressing these disparities can contribute to more equitable and effective cancer care delivery.

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## FOOTNOTES

**Author contributions:** Cordunianu AGV and Cochior D made the design and concept of the present study; Ganea G and Cordunianu AGV aquired the patient data and cofirmed authenticity of all raw data; Moldovan CA and Adam R performed data analysis and literature review; Cordunianu AGV and Moldovan CA drafted the initial manuscript; Cochior D and Moldovan CA revised the final manuscript; Cochior D critically revised the manuscript for intellectual content; All authors have read and approved the final manuscript.

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