

Insights into Tumor Localization and Associated Risk Factors in Upper Aerodigestive Tract Cancers

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ABSTRACT The upper aerodigestive tract encompasses the upper sections of both the digestive and respiratory systems, acting as a vital crossroads for essential functions such as eating, breathing, speaking, and smelling. This intricate region includes a network of ducts and cavities situated in the head and neck, making it crucial not only for nutrition and respiration but also for communication and sensory perception. These types of cancer are particularly daunting due to their potential for severe aesthetic and functional repercussions following treatment. The implications of these cancers can significantly disrupt a person's ability to eat, breathe, and speak normally, leading to profound impacts on quality of life.

Interestingly, over 90% of upper aerodigestive tract cancers are classified as squamous cell carcinomas, originating from the squamous cells that form the superficial layer of the mucosa in the head and neck region. Other types of malignancies found in this area include undifferentiated carcinomas, adenocarcinomas, and sarcomas, each with distinct characteristics and treatment challenges.

In our study, we aimed to explore the interplay of various factors influencing these cancers. We conducted a linear regression analysis examining variables such as profession, age, and socio-economic status, place of residence, gender, and weight. Additionally, we investigated key risk factors—including family history, medical history, smoking habits (both active and passive), history of alcoholism, surgical history, and the number of cigarette packs smoked per year—to assess their effects on the specific sites of tumors. By analyzing these variables, we hope to contribute valuable insights into the epidemiology of upper aerodigestive tract cancers, aiding in the identification of high-risk populations and the development of targeted prevention strategies. Understanding these dynamics is essential for advancing both treatment approaches and support systems for individuals affected by these challenging cancers.

Keywords: Upper Aerodigestive Tract; ENT Cancers; Squamous Cell Carcinoma; Tumor Site; Risk Factors; Linear Regression; Cancer Treatment.

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Word count: 5152 **Tables:** 05 **References:** 65

Received: 01 Sep, 2025, Manuscript No. OAR-25-171481;

Editor assigned: 04 Sep, 2025, PreQC No. OAR-25-171481 (PQ);

Reviewed: 22 Sep, 2025, QC No. OAR-25-171481;

Revised: 26 Sep, 2025, Manuscript No. OAR-25-171481 (R);

Published: 30 Sep, 2025

INTRODUCTION

Throughout history, distinct pathologies have significantly shaped public health responses and societal attitudes toward disease. Epidemics such as leprosy in the 11th century, the plague in the 14th century, syphilis in the 15th century, and tuberculosis in the 19th century have profoundly influenced healthcare strategies, leaving a lasting imprint on our collective memory [1,2].

As medical science has advanced especially through the development of vaccines and improved healthcare systems many infectious diseases have faded from public awareness. However, cancer has emerged as a pressing global health crisis, now ranking as the second leading cause of mortality worldwide, following cardiovascular diseases. According to GLOBOCAN 2020 estimates from the International Agency for Research on Cancer, approximately 19.3 million new cancer cases and nearly 10 million cancer deaths occurred globally in 2020. Among these, head and neck cancers, particularly those affecting the upper aerodigestive tract, pose significant challenges. Notably, female breast cancer has surpassed lung cancer as the most commonly diagnosed cancer, with an estimated 2.3 million new cases. Lung cancer remains the leading cause of cancer mortality, accounting for about 1.8 million deaths, while colorectal, prostate, and stomach cancers also contribute significantly to the overall cancer burden [3,4].

Oral cavity cancers are particularly alarming, representing about 10% of all cancer cases in the U.S. and exhibiting a five-year mortality rate of approximately 70% [5]. These cancers account for around 3% of all cancers diagnosed annually and have shown a troubling increase in incidence from 2007 to 2016, particularly for specific sites such as the base of the tongue, anterior tongue, gums, tonsils, and oropharynx [6]. In contrast, incidence rates have declined for cancers of the lip, floor of mouth, and other regions. This trend highlights the ongoing challenge posed by ENT cancers, which not only affect individual patients but also place considerable strain on healthcare systems. Effective management requires collaboration among various health professionals, including stomatologists, maxillofacial surgeons, otolaryngologists, and oral surgeons, all crucial for prevention, diagnosis, and treatment [7].

A comprehensive understanding of the cancer process, especially

in the oro-buccal region, is essential for effective intervention. This involves examining the global epidemiology of oral cancers and identifying key risk factors, particularly tobacco and alcohol use. The influence of these risk factors extends beyond simple associations; they can significantly affect tumor site localization within the upper aerodigestive tract. For instance, tobacco use has been linked to increased incidence of cancers in the oral cavity, pharynx, and larynx, while alcohol consumption often exacerbates the carcinogenic effects of tobacco [8]. Additionally, the anatomical features of the upper aerodigestive tract may contribute to the localization of tumors, making certain areas more susceptible to malignant transformations [9].

Recent findings emphasize the role of human papillomavirus (HPV) in the etiology of oropharyngeal cancers, complicating prevention efforts [10]. The rise in oral cavity and pharyngeal cancers has been attributed in part to HPV, suggesting a shift in causal factors beyond traditional tobacco and alcohol use. The GLOBOCAN data reveal significant disparities in cancer incidence and mortality rates between transitioned and transitioning countries, with rates for oral cavity cancers being 2- to 3-fold greater in transitioned nations. Death rates for female breast and cervical cancers are notably elevated in transitioning countries, underscoring inequalities in healthcare access and preventive measures [11].

In a related analysis of cervical cancer, global estimates for 2020 indicated approximately 604,127 cases and 341,831 deaths, with an age-standardized incidence of 13.3 per 100,000 women-years and a mortality rate of 7.2 per 100,000 women-years [11]. Geographical disparities were evident, with incidence rates ranging from 2.2 in Iraq to 84.6 in Eswatini. A clear socioeconomic gradient was observed: incidence was three times higher in low Human Development Index (HDI) countries compared to very high HDI countries, and mortality rates were six times higher [12]. Most countries showed a decline in cervical cancer incidence, stabilizing around 2005 in high-income nations, while some regions, particularly eastern Africa and Eastern Europe, experienced increases. The study emphasizes the ongoing burden of cervical cancer and the urgent need for improved screening and treatment services to address significant global inequalities in healthcare access. Looking ahead, the global cancer burden is projected to rise to 28.4 million cases by 2040, marking a 47% increase from 2020, particularly in transitioning countries due to demographic changes and increasing risk factors associated with globalization [13].

From early 2020 onward, epidemiological research has gained unprecedented attention due to the COVID-19 pandemic. Epidemiology has played a critical role in understanding disease distribution, assessing the scale of the pandemic, and shaping the global response [14]. This period has highlighted the politicized nature of epidemiological work and its historical significance. As a systematic effort to understand how disease affects different populations, epidemiology has informed a wide range of public health measures from quarantines to urban sanitation, meat inspections to cancer screening, and mass vaccinations to anti-smoking campaigns.

Epidemiological knowledge not only addresses health-related

issues but also profoundly influences social interactions, trade, travel, and urban planning in contemporary societies. The emphasis on understanding health as a lifetime accumulation of risks has fostered a perception of individual responsibility in risk reduction [15]. Thus, modern epidemiology has become integral to how societies conceptualize and manage health, shaping policy and public behavior.

In our study, we will utilize statistical analysis, specifically linear regression, to investigate the relationships between various tumor sites and contributing factors. This approach will enhance our understanding of the factors influencing oral cavity cancers, ultimately guiding more effective prevention and treatment strategies. By integrating the latest findings in cancer research and insights from epidemiology, we aim to contribute to global cancer control efforts and address the increasing impact of oral cavity cancers on public health, taking into account the quality of life, aesthetic consequences, and functional impact these cancers have on patients.

MATERIALS AND METHODS

Study Type and Setting

This retrospective study analyzed the medical records of patients diagnosed with upper aerodigestive tract cancers at the Oncology Department of Mohamed VI University Hospital in Marrakech, Morocco. The data collection period spanned from September 2020 to June 2021. This study setting is significant due to the growing incidence of head and neck cancers in Morocco, which has been attributed to factors such as tobacco and alcohol use, as well as viral infections like HPV [16].

Data Analysis

In this study, we utilized statistical analysis through linear regression to explore various cases in relation to the dependent variable, which is the site of the tumor. Linear regression is a statistical method that models the relationships between dependent and independent variables. It is widely used to describe and analyze data, facilitating predictions, forecasts, and estimates [17].

Using a supervised learning algorithm, we determined the linear relationship between the dependent variable and one or more explanatory variables. This approach is supported by recent findings indicating that linear regression can effectively identify risk factors associated with cancer outcomes [18].

For the implementation of the linear regression test, we employed SPSS version 25, sophisticated data analysis software developed by IBM. SPSS is classified as a premier statistical analysis tool, alongside others such as Stata, Minitab, Power BI, and Statistical. Its comprehensive features make it the reference software for statistical analysis, providing robust capabilities for data processing and interpretation. Moreover, the reliability of linear regression in cancer research has been established in various studies, showing its effectiveness in understanding complex relationships between variables, such as the correlation between lifestyle factors and cancer prognosis [19]. This methodological rigor is essential

in ensuring the validity and applicability of our findings in the context of upper aerodigestive tract cancers.

Definition of the Cancer Process

The cancer process begins with the intricate response of tissues to various external insults, such as chemical exposure, radiation, or viral infections. In most cases, normal cells possess adaptive mechanisms that allow them to restore equilibrium once the threat subsides. However, certain agents can induce genetic alterations that lead to permanent changes in cellular behavior, particularly in growth and differentiation. This phenomenon gives rise to neoplasms—abnormal growths that arise from genetic disorders transmitted from parent cells to their offspring. Neoplastic cells become autonomous, losing their ability to respond to regulatory signals that typically govern normal cell growth and function [20].

A collection of these neoplastic cells is termed a tumor, while the term "cancer" specifically refers to malignant neoplasms. Cancer is characterized by uncontrolled and autonomous cell proliferation, with the potential to invade surrounding tissues and metastasize to distant sites. This malignant behavior is a defining feature that distinguishes cancer from benign tumors, which are generally well-defined and do not spread beyond their local area [21].

The Cancer Cell

Cancer cells possess a unique set of characteristics that starkly differentiate them from their normal counterparts. These distinct traits arise from a series of genetic mutations and alterations that occur within the tumor clone, providing a selective advantage that facilitates unchecked growth and survival, often at the expense of surrounding healthy tissues. The following are key features of cancer cells:

- **Loss of Contact Inhibition:** Unlike normal cells, which halt proliferation in response to neighboring cells, cancer cells ignore these regulatory signals. This loss of contact inhibition leads to unregulated growth and the formation of dense tumor masses, contributing to tumor expansion and invasiveness [20].
- **Accelerated Proliferation:** Cancer cells exhibit an abnormal rate of division, allowing for rapid accumulation of tumor cells. This accelerated proliferation not only increases tumor mass but also enhances the likelihood of invasion into adjacent tissues and metastasis to distant sites [22].
- **Increased Plasticity and Mobility:** One of the hallmark traits of cancer cells is their ability to change shape and migrate. This plasticity enables cancer cells to invade surrounding tissues and disseminate throughout the body, complicating treatment efforts and facilitating the establishment of secondary tumors [23].
- **Cellular Morphological Abnormalities:** Cancer cells often present significant irregularities in their nuclei and cytoplasm, including enlarged nuclei, atypical shapes, and variations in cell size. These morphological changes are frequently associated with aggressive tumor behavior and poorer prognosis [24].
- **Antigenic Power:** Malignant cells have the capacity to develop clones with similar genetic profiles, allowing them to evade immune detection and foster tumor survival. This antigenic

variability complicates treatment strategies and poses challenges for effective immunotherapy [25].

Anatomical Context: The Upper Aerodigestive Tract

Cancers of the upper aerodigestive tract encompass a range of malignancies affecting critical structures such as the oral cavity, pharynx, and larynx. These regions are significant in the context of head and neck cancers due to their anatomical complexity and functional importance [26].

The Oral Cavity

At the forefront of the upper aerodigestive tract lies the oral cavity, a multifaceted space critical for initiating digestion and facilitating communication. It comprises the mobile tongue, which is essential for tasting, manipulating food, and forming speech; the floor of the mouth, which houses vital structures such as the submandibular glands; the gums, which provide support for the teeth; the inner cheeks, which assist in food movement; the lips, which serve as the gateway for food intake; and the velum, or soft palate, that plays a crucial role in swallowing and speech. This intricate structure not only aids in the mechanics of eating and speaking but also serves as a first line of defense against pathogens, making it a frequent site for cancers such as squamous cell carcinoma [27].

The Oropharynx

Descending from the oral cavity, the oropharynx acts as a critical junction in the aero-digestive tract. This area is composed of the palatine tonsils, which are part of the immune system, and the pillars of the fauces that mark the entry into the throat. The oropharynx also includes parts of the base of the tongue, a site that has gained prominence in recent years due to its association with human papillomavirus (HPV)-related cancers. As a crossroads for both food and air, the oropharynx is uniquely vulnerable to malignancies that can disrupt both swallowing and breathing [28].

The Larynx

Moving deeper into the upper aerodigestive tract, we find the larynx, a sophisticated structure that serves multiple essential functions. Comprising the epiglottis, which prevents food from entering the airway, and the vocal cords, which facilitate sound production, the larynx is instrumental in communication. This complex organ is also vital for protecting the lower airways during swallowing. However, it is susceptible to cancers that can significantly impair voice and respiratory function, leading to profound impacts on quality of life [29].

The Nasopharynx

Situated just above the soft palate, the nasopharynx is an extension of the nasal cavities and serves as a critical conduit for air and sound. It connects the nasal passages with the throat and contains lymphoid tissue, which can be involved in both immune

responses and malignancies. The nasopharynx is often affected by nasopharyngeal carcinoma, a cancer that poses unique challenges for detection and treatment due to its location and the subtlety of its initial symptoms [30].

The Hypopharynx

Lastly, the hypopharynx lies in front of the 5th and 6th cervical vertebrae and is comprised of the piriform sinuses. This area plays a vital role in the swallowing process, guiding food from the oropharynx into the esophagus. The hypopharynx is often a site for advanced cancers that may arise from prolonged exposure to risk factors such as smoking and alcohol use. Due to its position and the potential for late-stage diagnosis, cancers in this region can be particularly aggressive and challenging to treat [31].

Main Cancers in This Region

The primary cancers affecting the upper aerodigestive tract include:

- Squamous cell carcinoma of the oral cavity, oropharynx, larynx, and hypopharynx

- Nasopharyngeal cancer
- Cervical lymphadenopathy without a primary tumor, often linked to squamous cell carcinoma
- Cancers of the nasal and paranasal cavities
- Parotid gland cancer
- Tumors of the external auditory canal, including glomus tumors
- Orbital cavity tumors
- Thyroid cancer

Understanding these various cancer types is crucial for developing effective treatment strategies and improving patient outcomes. The interplay of risk factors such as family history, smoking, alcoholism, and socio-economic status plays a vital role in the epidemiology of these cancers, impacting not only survival rates but also the overall quality of life for affected individuals [32].

RESULTS AND DISCUSSION

Socio-demographic and clinical characteristics of the study population

In this study, 271 patients were diagnosed with cancer. The mean age of the patients was 56 years, with extremes ranging from 25 to 75 years. Almost a third of cases (29.89%) were between 56 and 65 years of age. The incidence of cancer was higher in men (69.74%) than in women (30.26%). With regard to patient location, we noted that the majority came from urban areas (76.01%), followed by rural areas (23.99%). With regard to socio-economic level, we observed that 85.61% of cases were covered by the “Ramedist” scheme, compared with 4.06% for those not covered. We also found that most patients had a profession (59.78%), while 37% did not. In terms of addictive habits, smoking was reported in

141 patients (52.03%). The highest percentage concerned patients using cigarettes+Hashish (94.70%)” was reported in 74 patients (52.48%), and alcohol consumption was observed in 37 patients (13.65%). Among cancer patients, 12.55% had a medical history, 7.38% a surgical history, and 51.66% a family history of cancer. According to the [Table 1], 66 patients had cancer in the oral cavity and 59 in the larynx. The statistical study shows that the treatment most frequently used by patients was applied in 92.62% of cases (251 patients).

Table 1: Socio-demographic and clinical characteristics of the study population.

Variables	Total Population 271 N (%)
Age Median [Q1-Q3]	
25-35	24 (8,86)
36-45	42 (15,50)
46-55	49 (18,08)
56-65	81 (29,89)
66-75	41 (15,13)
< 25	5 (1,85)
> 75	29 (10,70)
Adobe Garamond Pro	
Woman	82 (30,26)
Men	189 (69,74)
Adobe Garamond Pro	
Rural	65 (23,99)
Urban	206 (76,01)
Socio-economic level	
Mutualist	28 (10,33)
No ramedist	11 (4,06)
Ramedist	232 (85,61)
Profession	
With	162 (59,78)
Retreat	8 (2,95)
Without	101 (37,26)
Weight	60,45
Min	16,56
Max	86
Smoking	
No	130 (47,97)
Yes	141 (52,03)
Type	
Cigarettes	125 (94,70)
Cigarettes Hashish	3 (2,27)
Cigarettes+Kiff	4 (3,03)
Weaned	
No	67 (47,52)
Yes	74 (52,48)
Alcoholism	
No	234 (86,35)
Yes	37 (13,65)
ATCDs Medical	
With	34 (12,55)
Without	237 (87,45)
ATCDS Surgical	
With	20 (7,38)
Without	251 (92,62)
ATCDS Family	
With	140 (51,66)

Without	131 (48,33)
Site	
Tongue	25 (9,22)
Lip	15 (5,53)
the face	3 (1,11)
Thyroid	3 (1,11)
Nasal cavity	18 (6,64)
Floor of the mouth	6 (2,21)
Maxilla	19 (7,01)
cheek	11 (4,06)
Hypopharynx	13 (4,80)
Other site	15 (5,54)
Mouth of the esophagus	18 (6,64)
Larynx	59 (21,77)
Cavity	66 (24,35)
Classification TNM	
T1N0M0	2 (0,74)
T1N2M0	1 (0,37)
T2N0M0	28 (10,33)
T2N0M1	2 (0,74)
T2N1M0	6 (2,21)
T2N1M1	1 (0,37)
T2N2M0	10 (3,69)
T2N2M1	5 (1,85)
T2N3M0	2 (1,85)
T3N0M0	39 (14,39)
T3N0M1	1 (0,37)
T3N1M0	27 (9,96)
T3N1M1	3 (1,11)
T3N2M0	33 (12,18)
T3N3M0	3 (1,11)
T3N3M1	3 (1,11)
T4N0 M0	2 (0,74)
T4N1M0	23 (8,49)
T2N1M0	11 (4,06)
T4N1M1	3 (1,11)
T4N2M0	43 (15,87)
T4N2M1	8 (2,95)
T4N3M0	13 (4,80)
T4N3M1	2 (0,74)
Type of tumor	
T1	3 (1,11)
T2	54 (19,93)
T3	111 (40,96)
T4	103 (38,01)
Treatment	
Chemotherapy	251 (92,62)
Surgery	75 (27,68)
Brachytherapy	1 (0,37)
Exclusive radiotherapy	16 (5,90)
Post-operative radiotherapy	4 (1,48)

Multinomial logistic regression analysis

The difficulty in interpreting the effects of different factors lies in their close association with each other. In order to distinguish the variable with the most significant role from that which is merely a consequence of it, we carried out a logistic regression, enabling us to highlight the impact of each of the variables studied

on the tumor site [Table 2]. Shows that the regression model has a value of 3998.666, representing the variance explained by the model. In contrast, the value of 53794.360 indicates the unexplained variance. The associated p-value is 0.004, which is below the 0.05 threshold. This means that the regression model is statistically significant, indicating that the variables age, gender, socio-economic level, location, occupation and weight contribute significantly to explaining the variance of the dependent variable (tumor site).

[Table 3], show that only the “Age” variable is highly significant ($p = 0.00 < 0.05$) and has a moderate effect on tumor site. The other variables (gender, location, weight, socio-economic level and occupation) show no statistically significant effect ($p > 0.05$).

[Table 4], shows that the associated p-value is 0.060. This value is slightly above the usual threshold of 0.05, indicating that the regression model is not statistically significant at the 95% confidence level. This means that there is insufficient evidence to conclude that risk factors (family history, medical history, cigarette consumption, smoking, withdrawal, alcoholism, surgical history, number of packs per year, active/passive exposure to tobacco) significantly influence tumor site.

We note from [Table 5], that only the “Weaned” factor ($p < 0.05$) is significant for tumor site, while the other risk factors studied (Family history, Medical history, Cigarettes, Smoking, Non-smoker, Weaned, Alcoholism, Surgical history, Number of packs/year, Active, Passive.) are not ($p \geq 0.05$).

DISCUSSION

Several risk factors are associated with laryngeal malignancies, especially squamous cell carcinoma. It has been demonstrated that

Table 2: ANOVA test for Tumor Site.

ANOVA ^a					
Model	Sum of Squares	Df	Mean Square	F	Sig.
Regression	3998,666	6	666,444	3,233	,004 ^b
Residual	53794,360	261	206,109		
Total	57793,026	267			

a. Dependent Variable: Tumor site.

b. Predictors: (Constant), Age, Gender, Socio-economic level, location, Profession, Weight.

Table 3: Coefficients for Tumor Site.

Coefficients ^a					
Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
(Constant)	39,973	12,081		3,309	,001
Age	,233	,063	,243	3,693	,000
Gender	,189	2,064	,006	,091	,927
Location	-1,033	2,189	-,030	-,472	,637
Weight	-,343	,188	-,122	-1,819	,070
Socio-economic level	-2,546	1,452	-,106	-1,754	,081
Profession	-,101	,071	-,094	-1,412	,159

a. Dependent Variable: Tumor site.

Table 4: ANOVA test risk factors- Tumor Site.

ANOVA ^a					
Model	Sum of Squares	Df	Mean Square	F	Sig.
Regression	3824,572	11	347,688	1,810	,060 ^b
Residual	22671,436	118	192,131		
Total	26496,008	129			

a. Dependent Variable: Tumor site.

b. Predictors: (Constant), Family history, Medical history, Cigarettes, Smoking, Non-smoker, Weaned, Alcoholism, Surgical history, Number of packs/year, Active, Passive.

Table 5: Coefficients for Tumor Site-Risk Factors.

Coefficients ^a					
Model	Unstandardized Coefficients		Standardized Coefficients	T	Sig.
	B	Std. Error	Beta		
(Constant)	53,235	74,007		,719	,473
Smoking	-11,218	14,037	-,069	-,799	,426
Asset	-8,055	14,189	-,085	-,568	,571
Passive	1,990	19,666	,017	,101	,920
Cigarettes	,978	19,936	,006	,049	,961
Not smoked	1,122	,591	,175	1,897	,060
Number of packages/year	,156	,082	,172	1,897	,060
Weaned	7,433	2,626	,258	2,830	,005
Alcoholism	,052	2,656	,002	,020	,984
Medical background	-,021	,382	-,005	-,055	,956
Surgical history	-,381	,473	-,073	-,806	,422
Family history	-2,800	2,000	-,125	-1,400	,164

a. Dependent Variable: Tumor site.

these elements are crucial to the emergence of carcinogenesis. The intricate and multi-step process of carcinogenesis is typified by the squamous epithelium's cytologic and architectural modifications as well as successive cumulative genetic changes [33]. This process involves a number of agents, which result in mutations and the advancement of cellular transformation. Thus, in the current study, we examined the impact of the variables (weight, gender, place of residence, age, profession, and socioeconomic status) on the tumor site using the linear regression test. We proved that the tumor site is significantly impacted by these factors. The tumor site is greatly impacted by the risk variables (family history, medical history, smoking, cigarettes, active, passive, non-smoking, weaning, alcoholism, surgical history, and number of packets/year). We discussed about the specifics of our investment in the session below by contrasting it with previous research in the literature.

A number of scientific investigations have found that exposure to different carcinogens and a complicated interaction between genetic and environmental variables are the main causes of oral malignancies. Smoking, using smokeless tobacco (SLT) products, and drinking too much alcohol are among the preventable causes of 90% of oral malignancies [34–36]. Accordingly, the biggest risk factor for laryngeal cancer is tobacco use [37]. Throughout the 1950s, numerous investigations have shown a link between tobacco use and the occurrence of head and neck cancer [38]. Around 95% of individuals with laryngeal cancer in the United States smoke [39]. The particular risk for various forms of smoking is less known, but the carcinogenic effect of smoking on laryngeal cancer has been extensively researched [40]. The association

between smoking a cigar or a pipe and

developing laryngeal cancer is less clear because these individuals usually do not inhale smoke [41]. However, it has been shown that smoking tobacco increases the incidence of laryngeal cancer in a dose-response manner. In comparison to people who do not smoke or drink alcohol, the chance of acquiring laryngeal cancer is 177 times higher once alcohol usage and smoking are coupled [42]. Consequently, the risk of laryngeal cancer is multiplied by the combined harmful effects of alcohol and smoke.

Fortunately, the main known causes of malignancies of the aerodigestive tract are the consumption of alcohol and tobacco, both alone and in combination [43–46]. These two exposures have also been associated to cancers of the esophagus, larynx, pharynx, and mouth, and to a lesser degree, the stomach cardia. The degree of physical contact between the agent and target tissue may be a contributing factor in the apparent site-specific variation in the potency of these relationships [47]. A few investigations that have looked at the associations for other cell types have revealed more evidence of heterogeneity. Additionally, there seem to be varying levels of alcohol-tobacco interaction from one location to another, though this conclusion is complicated by the range of approaches that have been employed in various investigations.

Although there was a clear incidence of laryngeal carcinomas in the group under consideration, we discovered that patients who drank heavily had tumors that were primarily limited to the tongue, whereas individuals who did not drink had a longer distribution. Though the precise etiology is unknown, a number of characteristics may be risk factors for tongue cancer,

including advanced age, geographical region, family history, dietary deficiencies, transmissible diseases, and, of course, long-term alcohol and tobacco use [48]. Additionally, there is a lack of knowledge on the connection between alcohol use and tongue cancer growth. Chinese case-control research [49] investigating the relationship between alcohol use and the incidence of tongue cancer found no correlation with alcohol use. However, long-term alcohol use was associated with a slightly greater impact, indicating that alcohol may be a risk factor. On the opposing side, according to an alternate investigation[50], smoking, drinking, and eating appear to be the main causes of potential variations in risk factors between tongue cancer and cancers that develop outside in the oral cavity. remarkably, there is a chance that the molecular basis for the start of cancer in the oral cavity could be predisposing genetic factors. Genes linked to tongue cancer have been found to be differently regulated in patients with a history of alcohol and/or tobacco use compared to the non-habit population in the past[51] and more subsequently [52]. Besides, alcohol and tobacco use together significantly raise the risk of head and neck cancer. A non-smoker who consumes 10 glasses of wine averaged per day, or 1 liter of wine at 12.5° or the equivalent in terms of pure alcohol, is at risk for dental cancer. mouthwash multiplied by five in comparison to a nonsmoker who consumes fewer than 3.5 glasses daily. The risk is multiplied by six for a person who smokes more than 25 cigarettes and consumes fewer than 3.5 glasses of alcohol per day, as opposed to a person who does not smoke and consumes fewer than 3.5 glasses. In comparison to an individual who refrains from smoking and consumes fewer than 3.5 glasses per day, an individual who combined the two risk factors that is, smokes more than 25 cigarettes per day and drinks at least 10 glasses per day have a risk doubled by 103[53].

Interestingly, epidemiological research on the associations between alcohol, tobacco, and aerodigestive malignancies has been conducted for about 50 years [54–58]. The results of the large amount of material that has been produced have typically been consistent, but without thorough examination, it is challenging to draw more than the most fundamental conclusions due to variations in presentation and methodology. It is difficult for anyone trying to bring the literature together into a cohesive picture because of differences in reference group definitions, drinking and smoking habit assessments, and just the different study sizes.

The combination of factors associated with lifestyle and genetic vulnerability leads to cancer. Age is a factor in cancer diagnosis; following the age of conception, the frequency of cancer rises noticeably. Sensitivity to toxins and nutrients is a significant risk factor for certain types of cancer. As a factor in body structure and growth, nutrition also affects the risk of cancer, either immediately through food carcinogens or indirectly through the hormonal and metabolic reactions to fat and growth. In the paragraph that follows, we highlighted the impact of the most important lifestyle factors that affect a patient's cancer appearance, such as age, occupation, oral hygiene, and diet. Firstly, we discussed how the age difference of a patient can influence the appearance of cancer. For instance, a 70-year-old without any risk factors (alcohol, smoke, etc.) has a roughly 100-fold higher chance of getting cancer than a 20-year-old. Despite being a natural process, senescence causes tissue

alterations that lead to the development of numerous illnesses. Because of the biophysiological changes associated with aging, which are characterized by an imbalance between the organism's repair and degradation processes, an imbalance favoring the latter, older adults do in fact present a more favorable environment for the development of precancerous and cancerous lesions.

In addition, asbestos exposure raises the risk of laryngeal cancer. According to epidemiological evidence, formaldehyde exposure and nasopharyngeal cancer are causally related. Polycyclic hydrocarbon exposure at work increases the incidence of laryngeal and mouth malignancies. Nasopharyngeal carcinoma is also linked to wood dust exposure. Certain HLA system indicators (HLA-A2, B2, Bw46) may indicate a genetic predisposition to nasopharyngeal cancer. Ethmoid adenocarcinomas are known to occur in the shoe industry as well as among people who handle nickel and wood. Farmers who use pesticides and fertilizers, as well as professionals working in general metallurgy or general mechanics, are more likely to have squamous cell carcinomas[53].

Furthermore, the literature states that some teams believe it to have a triggering role[59]. Nevertheless, there is no evidence from any recent study that better oral hygiene is associated with a lower incidence of oral cancer. By boosting the oral flora, poor hygiene may be a contributing factor to the development of oral malignancies. This carcinogen's oral concentration is raised by the latter, which actively contributes to the breakdown of ethanol into acetaldehyde [60].

Correspondingly, one significant problem is that obesity raises the risk of cancer and several other chronic illnesses [61,62]. A median adult BMI of 21–23 kg/m² is presently recommended by the World Cancer Research Fund's (WCRF) Public Health Goals, depending on the normal range for different populations [63]. In this context, numerous epidemiological studies have examined the influence of nutrition. The most frequently observed effect of eating a lot of fruit and vegetables is a reduction in cancer of the pharynx and oral cavity [64]. Cancer risk is greatly increased by a Western-style diet that is high in calories, fats, and animal proteins and is frequently paired with a sedentary lifestyle. On the other hand, there is a lower chance of acquiring cancer of the mouth, larynx, esophagus, or even the throat and stomach if you exercise, maintain a healthy weight, and regularly eat fresh fruits and vegetables [65].

CONCLUSION

In conclusion, the prevention of head and neck cancers primarily relies on significantly reducing the consumption of tobacco and alcohol. These substances, especially when consumed together, greatly increase the risk of developing these types of cancers. Among the preventive strategies, increasing cigarette prices has proven effective in discouraging consumers, particularly younger individuals, thereby reducing tobacco sales. However, for a comprehensive prevention approach, it is essential to combine this measure with awareness campaigns and support policies for those who wish to quit smoking or drinking. A holistic approach, incorporating actions on product pricing, awareness, and cessation support, can provide tangible results and contribute to reducing

the incidence of head and neck cancers.

ACKNOWLEDGMENTS

In this study, all authors declare no conflict of interest and no financial support of a company or a financial organization.

FUNDING

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The publication of this article was made possible by the authors' contributions and their affiliation with University Hospital Mohamed VI, Marrakech.

Source(S) of Support/Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The publication of this article was made possible by the authors' contributions and their affiliation with University Hospital Mohamed VI, Marrakech.

Disclosure of Relationships and Activities

In this study, all authors declare no conflict of interest.

Ethical Issues

Approval for the study was granted by the Ethics Committee of the University Hospital of Marrakech under the number 65/2025. Additionally, confidentiality and anonymity were respected during the data collection.

ACKNOWLEDGEMENTS

In this study, all authors declare no conflict of interest and no financial support of a company or a financial organization.

AUTHORS' CONTRIBUTIONS

RE contributed to conception, design, data and statistical analysis. HJ and AE contributed to interpretation of data. The draft of manuscript was revised by RE, HJ and AE. All authors read and approved the final manuscript.

Data Availability Statements

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

REFERENCES

1. Smith RT, Guinnane P, Wallis C, Sarasúa L, Taylor S. An introduction to the history of infectious diseases, epidemics and the early phases of the long-run decline in mortality. *Econ. Hist. Rev.* 2020; 3: 1–19.
2. Rose PI, Frank MS. *Epidemics and Society : From the Black Death to the Present*, Society. 2020; 57: 478–480.
3. Bray F, Ferlay J, Soerjomataram I. Global Cancer Statistics 2018 : GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries, *Ca Cancer J Clin.* 2018; 68: 394–424.
4. Henley SJ, Gallaway MS, Singh SD, Lunsford B, Momin B, et al. A Report from CDC: Lung Cancer among Women in the United States, *J Womens Heal. (Larchmt).* 2019; 27: 1307–1316.
5. Wangmo DT, Vogel P, Zbaeren HC. Thoeny Cancer of the oral cavity and oropharynx, *Cancer Imaging* 2010; 10: 62–72.
6. Miller KD, Fuchs HE, Jemal A. Cancer Statistics 2021, *Ca Cancer J Clin* 2021; 71: 7–33.
7. Fitch MI, Longo CJ, Javan R. Cancer patients' perspectives on financial burden in a universal healthcare system : Analysis of qualitative data from participants from 20 provincial cancer centers in Canada, *Patient Educ. Couns* 2021; 104: 903–910.
8. Vecchia CL. Cancer risk associated with alcohol and tobacco use : focus on upper aero-heal. *Risks* 2006; 29: 193–198.
9. Pai WH, Westra SJ. Molecular Pathology of Head and Neck Cancer: Implications for Diagnosis, Prognosis, and Treatment, *NIH Public Access* 2013; 4: 49–70.
10. Pan CN, Issaeva WG. Yarbrough, HPV-driven oropharyngeal cancer : current knowledge of molecular biology and mechanisms of carcinogenesis, *Cancers Head Neck* 2018; 3: 1–11.
11. Singh DJ, Vignat V, Lorenzoni M, Eslahi O, Ginsburg B, et al. Global estimates of incidence and mortality of cervical cancer in 2020 : a baseline analysis of the WHO Global Cervical Cancer Elimination Initiative, *Lancet Glob. Heal* 2020; 11: e197–e206.
12. Vaccarella S, Lortet-tieulent J, Plummer MS, Franceschi FB. Worldwide trends in cervical cancer incidence : Impact of screening against changes in disease risk factors, *Eur. J. Cancer* 2013; 49: 3262–3273.
13. Satish Kumar KM, Chaturvedi P, Stephen DS, Mathur P. Cancer incidence estimates for 2022 & projection for 2025 : Result from National Cancer Registry Programme, India, *Indian J Med Res* 156; 2025: 598–607.
14. Jefferson S, Kumar S. Editorial : SARS-CoV-2 : virology, epidemiology, diagnosis, pathogenesis, and control, *Front. Viral* 4; 2024: 19–22.
15. Mukherjee A. Understanding Emerging Epidemics social and political approaches 2024; 10.
16. Reffai A, Mesmoudi M, Derkaoui T, Nourouti NG, Barakat A, et al. Epidemiological Profile and Clinicopathological Therapeutic and Prognostic Characteristics of Nasopharyngeal Carcinoma in Northern Morocco, *Cancer Control* 2021; 28: 1–2.
17. Pearce SE, Richards SM, Patel KA, Pariser SG, Eggener JJ. Statistical Methods in the Cancer Surveillance Research Program (SRP), *J Epidemiol* 2011; 176: 347–56.
18. E Veer, Oijen MGH Van, Laarhoven HWM Van. The Use of Network Meta-Analysis in Clinical Oncology, *Front. Oncol.* 2019; 822.
19. Petrova D, Maria J, Poll M, Vicente D. Public Perceptions of the Role of Lifestyle Factors in Cancer Development : Results from the Spanish Onco-Barometer 2020, *Int. J. Environ. Res. Public Health* 2021; 18: 10472.
20. Hanahan D, Weinberg RA. Hallmarks of Cancer: The Next Generation *Cell* 2011; 144: 646–674.
21. Patel A. Benign vs Malignant Tumors, *Technol. Networks* 2022; 6: 1488–1488.
22. Liao M, Yao D, Wu L, Luo C. Targeting the Warburg effect : A revisited perspective from molecular mechanisms to traditional and innovative therapeutic strategies in cancer, *Acta Pharm. Sin. B* 2024; 14: 953–1008.
23. Bayik D, Lathia JD. Cancer stem cell-immune cell crosstalk in tumour progression, *Nat. Rev. Cancer* 2021; 21: 526.
24. Weigelt B, Geyer FC, Reis-filho JS. Histological types of breast cancer : How special are they. *Mol. Oncol.* 2010; 4: 192–208.
25. Chen DS, Mellman I. Elements of cancer immunity and the cancer – immune set point, *Review* 2017; 541: 321.
26. Siegel RL, Miller KD. Cancer Statistics , 2019, *CA CANCER J CLIN* 2019; 69: 7–34.
27. Shenoy SKCA. Quality of Life in Head and Neck Cancer Patients, *Int. Soc. Qual. Life Res. Abstr. Contrib. Pap.* 2016; 4: 17–18.
28. Chaturvedi AK, Engels EA, Pfeiffer RM, Hernandez BY, Xiao W, et al. Human Papillomavirus and Rising Oropharyngeal Cancer Incidence in the United States. *J Ournal C Linical O Ncology* 2011; 29: 4294–4301.
29. Silveira A, Monteiro E, Sequeira T. Head and Neck Cancer : Improving Patient-Reported Outcome Measures for Clinical Practice, *Curr. Treat. Options in Oncol* 2018; 19: 59.
30. Wei WI, Sham JST. Nasopharyngeal carcinoma, *Seminars* 2005; 365: 2041–2054. Gormley M, Creaney G, Schache A, Ingarfield K, Conway DI. Reviewing the epidemiology of head and neck cancer : definitions, trends and risk factors, *Head Neck Cancer* 2022; 233: 780–786.
31. Wild BW, Weiderpass CPE. Stewart World Cancer Report for cancer prevention Cancer research, Lyon. 2020.
32. Cancerization F, Califano J, Van Der Riet P, Westra W, Nawroz H, et al. Sidransk, Genetic Progression Model for Head and Neck Cancer : Implications for, Cancer research 1996; 56: 2488–2492. [Google Scholar] [PubMed]
33. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, et al. Cancer incidence and mortality worldwide : Sources , methods and major patterns in GLOBOCAN 2012, *Int. J. Cancer* 2015; 136: E359–E386.
34. France L. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans VOLUME 89 Smokeless Tobacco and Some Tobacco-specific N -Nitrosamines Smokeless Tobacco and Some, World Health Organization International Agency for Research on Cancer. 2007.
35. Asthana R, Labani S, Kailash S, Sinha U, Mehrotra DN. Association of Smokeless Tobacco Use and Oral Cancer : A Systematic Global Review and Meta-Analysis, *Nicotine Tob. Res.* 2018; 1–10.
36. Medical C, Accreditation E, C. Nursing, E. Accreditation, an Update on Larynx Cancer, *Ca Cancer J Clin* 2017; 67: 31–50.
37. Liberale CD, Soloperto A, Marchioni D, Monzani L, Sacchetto. Updates on Larynx Cancer : Risk Factors and Oncogenesis 2023.
38. Ramsey T, Guo E, Svider PF, Lin H, Syeda S, et al. Laryngeal Cancer : Global Socioeconomic Trends in Disease Burden and Smoking Habits, *Laryngoscope* 2018; 128: 2039–2053.
39. Ramroth H, Dietz A, Becher H. Intensity and Inhalation of Smoking in the Aetiology of Laryngeal Cancer, *Int. J. Environ. Res. Public Heal.* 2011; 8: 976–984.
40. Henley SJ, Thun MJ, Chao A, Calle EE. Association between Exclusive Pipe Smoking and Mortality from Cancer and Other Diseases, *J. Natl. Cancer Inst.* 2004; 96: 853–861.
41. Bilano K, Gilmour VS, Moffiet T, d'Espaignet ET, Stevens GA, et al. Global trends and projections for tobacco use, 1990–2025: an analysis of smoking indicators from the WHO Comprehensive Information Systems for Tobacco Control, *Lancet* 2015; 385: 966–976.
42. Lyon F. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Report of the Advisory Group to Recommend Priorities for IARC Monographs during 2015 – 2019, *Int. AGENCY Res. Cancer.* 2019.

43. France L. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans VOLUME 83 Tobacco Smoke and Involuntary Smoking, WORLD Heal. Organ. Int. AGENCY Res. CANCER 2004; 83: 1473.
44. Zeka A, Gore R, Kriebel D. Effects of alcohol and tobacco on aerodigestive cancer risks : a meta-regression analysis, *Cancer Causes Control* 2003; 14: 897–906. [Crossref] [Google Scholar] [PubMed]
45. Fiore M, Minni A, Cavalcanti L, Raponi G, Puggioni G, et al. The Impact of Alcohol Consumption and Oral Microbiota on Upper Aerodigestive Tract Carcinomas : A Pilot Study, *Antioxidants* Artic. 2023; 12:
46. Tuyns LAJ, Esteve J, Raymond L, Berrino F, Benhamou E, et al. Cancer Of The Larynx/Hypopharynx, Tobacco And Alcohol: Iarc International Case-Control Study in Turin and Varese (Italy), Zaragoza and Navarra (Spain), Geneva (Switzerland) and Calvados (France), *Int. J. Cancer*. 1988; 491: 483–491.
47. Moore SR, Johnson NW, Pierce AM, Wilson DF. The epidemiology of mouth cancer : a review of global, *Oral Dis*. 2000; 6: 65–74. [Crossref] [Google Scholar] [PubMed]
48. Holford T, Chen Y, Jiang P, Zhang B, Boyle P. Risk of Tongue Alcohol Cancer Associated with Tobacco Smoking Consumption : a Case-Control Study, *Oral Oncol*. 1997; 33: 82–85. [Crossref] [Google Scholar] [PubMed]
49. Franceschi RS, Barra S, La Vecchia C, Bidoli E, Negri E. Talamini, Risk factors for cancer of the tongue and the mouth A case-control study from., *Cancer* 1992; 70: 2227–2233.
50. Donoff RB, Sciences D, Surgery MMG. Hospital, *Molecular Biology of Human Oral Cancer*, *Crit. Rev. Oral Biol. Med*. 1996; 7: 319–328.
51. Zhao YIN, Fu D, Xu C, Yang J, Wang Z. Identification of genes associated with tongue cancer in patients with a history of tobacco and / or alcohol use, *Oncol. Lett*. 2017; 13: 629–638.
52. Aupérin A, Hill C. Épidémiologie des carcinomes des voies aérodigestives supérieures Epidemiology of head and neck carcinomas, *Cancer/ Radiothérapie* 2019; 9: 1–7.
53. Wynder RM, Bross EL, Feldman EJ. A study of the etiological factors in cancer of the mouth., *Cancer* 1957; 10: 1300–1323.
54. Keller M, Terris AZ. A study of cases of cancer of the mouth and pharynx showed that such cancers are associated with cirrhosis of the liver, and independently with heavy alcohol consumption and smoking . These findings occur much less frequently among Jews. The authors con, *Am. J. Public Heal. Nations Heal*. 1965; 55: 1578-1585.
55. Rothmant K, Keller A. The Effect of Joint Exposure to Alcohol and Tobacco On Risk Of Cancer Of The Mouth And Pharynx. *J Chron Dis* 1972; 25: 711–716.
56. Wynder E, Bross EL. A Study of Environmental Factors in Cancer of the Larynx, *Cancer* 1955; 30.
57. Wynder L, Ross J. A Study Of Etiological Factors In Cancer Of The Esophagus, *Cancer* 1991; 14: 389–413.
58. Orbak R, Bayraktar C, Kavrut F. Poor oral hygiene and dental trauma as the precipitating factors of squamous cell carcinoma, *Oral Oncol. EXTRA* 41 (2005) 109–113. Rouers M, Truntzer P, Dubourg S, Guihard S, Antoni D, Noël G. Dental state in patients with head and neck cancers. *Cancer/Radiotherapy*, 2015; 19: 205–210.
59. Calle EE, Rodriguez C, Walker-thurmond K, Thun MJ. Overweight, Obesity, and Mortality from Cancer in a Prospectively Studied Cohort of U.S. Adults, *N Engl J Med* 2003; 348: 17.
60. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body-mass index and incidence of cancer : a systematic review and meta-analysis of prospective observational studies, *Lancet* 2007; 371: 569–578.
61. Pergola GD, Silvestris F. Obesity as a Major Risk Factor for Cancer, *J. of Obesity* 2013; 2013: 291546.
62. Mario F, Medica S. Diet diversity and gastric cancer, *Int. J. Cancer* 1997; 257: 255–257.
63. Kushi MJ, Byers LH, Doyle T, Bandera C, McCullough EV, Gansler MT. Thun, American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention : Reducing the Risk of Cancer with Healthy Food Choices and Physical Activity. *CA Cancer J Clin* 2006; 56: 254–281.