We are IntechOpen,
the world's leading publisher of
Open Access books
Built by scientists, for scientists

6,900
Open access books available

185,000
International authors and editors

200M
Downloads

Our authors are among the

154
Countries delivered to

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities

CLARIVATE ANALYTICS

BOOK
CITATION
INDEX

INDEXED

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

4

A Literature Analysis
of the Risk Factors for Oral Cancer

Shih-An Liu
National Yang-Ming University, Taichung Veterans General Hospital
Taiwan, R.O.C.

1. Introduction

Oral cancer is one of the top ten most common cancers in men. It is estimated that 190,000 new oral cavity cancer cases were diagnosed in 2008 worldwide with 83,000 deaths (Ferlay et al., 2010). In Taiwan, oral cancer has been one of the top 10 causes of death from cancer since 1991. According to the annual report from the Department of Health of the Executive Yuan, the death toll for oral cancer in males has been increasing at a surprising rate (Liu et al., 2006). Although advances in the treatment of oral cancers have been made in the last four decades, benefits have not been reflected in mortality figures. Therefore, primary prevention such as cessation of tobacco smoking and alcohol consumption along with early detection are necessary control procedures to improve the prognosis for oral cancer (Ramadas et al., 2003). However, it is crucial to identify relevant risk factors for contracting oral cancer before implementation of prevention programs. Here, we review the relevant literature and critically appraise the risk factors for contracting oral cancer.

2. Materials and methods

Web-based exploration of electronic resources was carried out to screen published literature. We searched for relevant articles (published up to May 2011) in the Medline/PubMed database. These searches included the use of free text and index terms, such as "risk factor", "oral cancer" and "head/neck cancer", in order to expand the number of potentially pertinent studies retrieved. Furthermore, we checked the relevant references cited in the retrieved articles for further studies to review. The levels of evidence and grades of recommendation of the cited studies are listed in Table 1. The process of article selection is summarized in Figure 1.

3. Risk factors for contracting oral cancer

All relevant risk factors in the literature are listed in Table 1. Further description of risk factors for oral cancer are discussed below.

3.1 Lifestyle factors

The etiology of oral cancer involves multiple factors and the most important are life style factors, such as cigarette smoking, alcohol consumption and betel quid chewing.
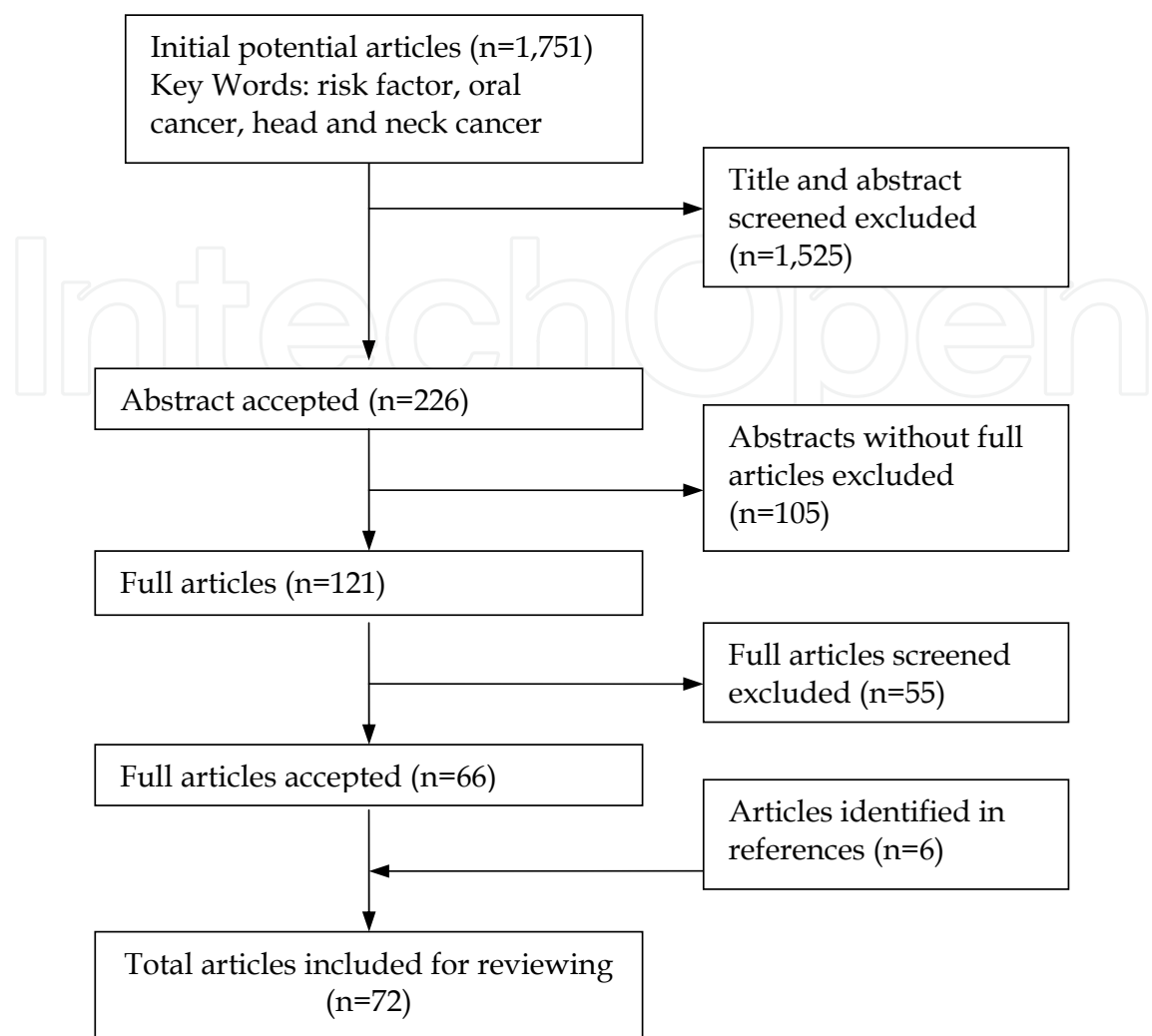
```
┌─────────────────────────────────┐
│ Initial potential articles      │
│ (n=1,751)                       │
│ Key Words: risk factor, oral    │
│ cancer, head and neck cancer    │
└─────────────────────────────────┘
               │          ┌──────────────────────┐
               │─────────▶│ Title and abstract   │
               │          │ screened excluded    │
               │          │ (n=1,525)            │
               ▼          └──────────────────────┘
┌─────────────────────────────────┐
│ Abstract accepted (n=226)       │
└─────────────────────────────────┘
               │          ┌──────────────────────┐
               │─────────▶│ Abstracts without    │
               │          │ full articles        │
               │          │ excluded (n=105)     │
               ▼          └──────────────────────┘
┌─────────────────────────────────┐
│ Full articles (n=121)           │
└─────────────────────────────────┘
               │          ┌──────────────────────┐
               │─────────▶│ Full articles        │
               │          │ screened excluded    │
               │          │ (n=55)               │
               ▼          └──────────────────────┘
┌─────────────────────────────────┐
│ Full articles accepted (n=66)   │
└─────────────────────────────────┘
               │          ┌──────────────────────┐
               │◀─────────│ Articles identified  │
               │          │ in references (n=6)  │
               ▼          └──────────────────────┘
┌─────────────────────────────────┐
│ Total articles included for     │
│ reviewing (n=72)                │
└─────────────────────────────────┘
```

Fig. 1. Results of literatures search. The figure illustrates the whole process of searching for articles for inclusion in this review.

3.1.1 Tobacco smoking

Data from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program revealed state-specific increases in oral cancer in United States. Further analysis indicated such states had comparatively higher percentages of smokers currently, as well as historically (Bunnell et al., 2010). It was estimated that a betel quid-chewing patient consumes 310,000 pieces of betel quid and a smoking patient consumes 14,000 packs of cigarettes before the diagnosis of oral cavity cancer on average. Besides, betel quid chewer and cigarette smoker were more prone to be diagnosed with oral cavity cancer at a younger age than abstainers (Tsai et al., 2009). Furthermore, heavy smoker were not only more likely to be diagnosed at a younger age but also at an advanced stage. Apart from active smoking, patients who were exposed to passive smoke were also found to have higher odds ratios (1.62 ~ 2.46) for contracting oral cavity and oropharynx cancers in a hospital-based case control study (Lee et al., 2009). The odds ratios or relative risks for contracting oral cancer among cigarette smoker, alcohol drinkers, or betel quid chewers are summarized in Table 2.

Risk factors	Grade of recommendation	Level of evidence
Lifestyle factors		
Cigarette smoking	A ~ B	1c ~ 3b
Alcoholic consumption	B	2b ~ 3b
Betel quid chewing	B	2b ~ 3b
Genetic factors	B	2b ~ 3b
Infectious factors	B	3a ~ 3b
Environmental factors	B	2b ~ 3b
Dietary factors	B	2b ~ 3b
Socio-economic factors	B	3a ~ 3b
Ethnicity and race	B	2b ~ 3b
Others	B	2b ~ 3a

Table 1. Relevant risk factors for contracting oral cancer in the literature

Variable	Odds ratios or Relative risk (95% CI[a])	Study design	Reference
Smoking			
Cigarette smoking	8.4 (3.5 ~ 20.4)	Case-control	Ko et al., 1995
Current smoker	6.41 (3.32 ~ 12.37)	Case-control	Castellsagué et al., 2004
Habitual smoker	4.65 (2.74 ~ 7.89)	Cohort	Yen et al., 2008
> 30 pack-years	2.9 (1.8 ~ 4.5)	Case-control	Smith et al., 2010
Smoker	1.68 (1.00 ~ 2.81)	Case-control	Ihsan et al., 2011
Bidi smoking	2.6 (1.4 ~ 4.9)	Cohort	Jayalekshmi et al., 2011
> 40 pack-years[b]	8.46 (6.22 ~ 11.50)	Case-control	Lee et al., 2011
>= 60 pack-years	10.1 (6.1 ~ 16.7)	Case-control	Lubin et al., 2010
Former smoker[b]	5.49 (4.06 ~ 7.41)	Case-control	Szymanska et al., 2011
Alcohol			
Alcohol drinking	3.2 (1.8 ~ 5.6)	Case-control	Ko et al., 1995
Current drinker	3.46 (1.88 ~ 6.35)	Case-control	Castellsagué et al., 2004
Habitual drinker	0.95 (0.29 ~ 3.11)	Cohort	Yen et al., 2008
>= 30 grams per day[c]	1.92 (1.08 ~ 3.40)	Cohort	Shanmugham et al., 2010
> 21 drinks per week[d]	4.8 (2.8 ~ 8.3)	Case-control	Smith et al., 2010
Alcohol consumption	1.71 (1.20 ~ 2.44)	Case-control	Li et al., 2011
Alcohol drinker[b]	4.62 (3.39 ~ 6.28)	Case-control	Szymanska et al., 2011
Betel quid			
Betel chewing	8.5 (4.4 ~ 16.2)	Case-control	Ko et al., 1995
Habitual chewer	10.97 (3.22 ~ 37.34)	Cohort	Yen et al., 2008
Chewer	12.52 (5.45 ~ 28.77)	Cohort	Wen et al., 2010
Chewer	1.85 (1.02 ~ 3.33)	Case-control	Ihsan et al., 2011

All use abstainers as reference group

[a] CI: confidence interval

[b] Including oral cavity and oropharynx patients

[c] Women only

[d] One drink was equivalent to a 12-oz can or a bottle of beer, 4 oz glass of wine, or 1.5 oz shot of hard liquor

Table 2. The association of smoking, alcoholic consumption and betel quid chewing and the risk of contracting oral cavity cancer

Tobacco contains N-nitroso compounds which are well-known carcinogens. In addition, cigarette smoke condensate has the capacity to activate nuclear factor kappa-B in squamous cell lines. Nuclear factor kappa-B is a transcription factor and has been implicated in the regulation of many proinflammatory pathways, which might be one mechanism leading to carcinogenesis (Rohrer et al., 2010). Other tobacco-generated carcinogens include tobacco-specific nitrosamines (TSNAs, e.g. NNN, NNK, NAT and NAB), and free radicals that can inhibit antioxidant enzymes (such as, glutathione-S-transferase, glutathione reductase, superoxide dismutase, catalase, and glutathione peroxidase) (Scully, 2011). This specific antioxidant enzyme activity loss renders the oral epithelial cells more vulnerable to the harmful effects of both thiocyanate ions and hydroxyl free radicals produced by residual H_2O_2 in the presence of salivary redox-active metal ions. It has been demonstrated that thiocyanate ions and free radicals may adversely react with DNA, thus paving the way for progression of oral cancer (Reznick et al., 2003).

3.1.2 Alcohol consumption

Although alcoholic consumption is often cited as a known risk factor of oral cavity cancer (Altieri et al., 2004; Scully, 2011; Szymańska et al., 2011), some studies did find alcohol was not associated with an elevated risk of oral cavity cancer (Takács et al., 2011; Yen et al., 2008). One possible explanation for the seeming contradiction may be that different studies defined alcohol consumption differently. Also, not all studies collected quantitative data on alcoholic consumption. Furthermore, the different alcohol-drinking profiles of various regions made the comparisons among studies more complicated. On the other hand, a previous case control study found a lower risk of oral cavity cancer in postmenopausal women with moderate alcoholic consumption (Takács et al., 2011). The beneficial systemic changes, namely the increased insulin sensitivity and elevated estrogen levels may explain the protective effects in these latter groups of cases.

Ethanol may work as a carcinogenic initiator or as a promoter that enhances permeability of cells to other environmental carcinogens, such as cigarette smoke. Ethanol is oxidized to acetaldehyde mostly through alcohol dehydrogenase and, to a lesser extent, cytochrome P450 enzymes in chronic drinkers (Lubin et al., 2009). Acetaldehyde is classified as "carcinogenic to humans" (IARC Group 1) by the International Agency for Research on Cancer (IARC) (Lachenmeier et al., 2011). Acetaldehyde not only induces DNA-protein cross-linking and DNA interstrand cross-linking, but also interferes with DNA repair mechanism by inhibiting repair enzyme. Apart from alcoholic consumption, acetaldehyde may also be produced by oral bacterial flora in patients with poor dentition or poor oral hygiene (Homann et al., 2000). A previous study found that short-term salivary acetaldehyde increased due to direct exposure to alcoholic beverages (Lachenmeier et al., 2011). This may suggest a possible mechanism to explain the greater risk for oral cavity cancer associated with alcoholic consumption.

3.1.3 Betel quid chewing

Betel quid is one of the most commonly used psychoactive substances. It has been estimated that there are 600 million betel quid chewers worldwide (Wen et al., 2010). People who chew betel quid but do not smoke cigarettes or consume alcohol were reported to have an odds ratio of 10.97 (95% confidence interval: 3.22-37.34) for contracting oral cancer (Yen et al.,

2008). Another case-control study found betel quid chewer had an odds ratio of 6.9 (95% confidence interval: 3.1-15.2) for developing oral cancer after adjustment for smoking and drinking alcohol (Ko et al., 1995).

Arecoline, the major alkaloid of areca nut, has been known to induce cytotoxicity and genotoxicity in various systems (Lin et al., 2011). It is also mutagenic in both bacteria and mammalian cells (Chang et al., 2001). Arecoline was found to inhibit P53, repress DNA repair, and trigger DNA damage response in human epithelial cells via an *in-vitro* study (Tsai et al., 2008). Chewing betel quid induces local irritation and trauma in the oral mucosa, leading to chronic inflammation, oxidative stress, and cytokine production, and the traumatic wound offers easier access to the system for carcinogens contained in betel quid (Wen et al., 2010). Betel quid chewing not only causes genomic instability, but also has a close relationship with cell-mediated immunity, which could play a role in the malignant transformation of oral mucosa (Yen et al., 2008).

3.1.4 Synergistic effect

Many studies have found that there is a synergic effect of cigarette smoking, alcoholic consumption, and betel quid chewing in carcinogenesis of oral cavity mucosa (Castellsagué et al., 2004; Chang et al., 2001; Ko et al., 1995; Szymańska et al., 2011; Wen et al., 2010; Yen et al., 2008). Patients who smoked and also consumed alcohol had an odds ratio of 9.03 for contracting oral cavity cancers, whereas patients who only smoke or only consumed alcohol had odds ratios of 4.65 and 0.95, respectively when compared with abstainers (Yen et al., 2008). *In vitro*, the addition of extracellular nicotine worked synergistically on the arecoline-induced cytotoxicity and this may partially explain why those who chew betel quid and smoke cigarette are at great risk of contracting oral cancer (Chang et al., 2001).

3.2 Genetic factors

Genetic instability, either spontaneous or mutagen induced, has been regarded as a predisposing factor for neoplastic transformation (Patel et al., 2010). Cancer is the result of DNA mutations occurring spontaneously and from the action of different mutagens. A sequence of genetic changes leads finally to loss of growth control and immortality (Scully, 2011). Together with these changes are mechanisms that metabolise carcinogens, repair DNA damage, control growth, and defend the human body against cancer. The development from an ordinary healthy cell to a pre-malignant or a potentially malignant cell is called oncogenesis (carcinogenesis). The level of chromatin breaks induced by a mutagen challenge may serve as an indicator of an individual's capacity to repair damaged DNA. A previous study showed that mean level of chromosomal aberrations was higher in oral cancer patients when compared with that of healthy controls (Patel et al., 2010). A dose relationship between lifetime tobacco exposure and chromosomal aberrations was also found in aforementioned study. Apart from healthy tissues, genomic imbalances in premalignant lesion tissues also had a strong association with malignant transformation (Garnis et al., 2009).

3.2.1 Epidermal growth factor receptor

The epidermal growth factor receptor (EGFR) is the cell-surface receptor for members of the epidermal growth factor family (EGF-family) of extracellular protein ligands. Increased or

aberrant expression of the EGFR or its ligands may lead to many processes important for tumor growth, including cell proliferation, survival, angiogenesis, invasion, and metastasis (Janmaat & Giaccone, 2003). A pervious study investigating EGFR gene in oral premalignant lesion specimens found that increased EGFR gene copy number was associated with higher risk of oral cancer (Taoudi Benchekroun et al., 2010). Other studies found significant increases in EGFR copy number and EGFR immuno-reactivity in oral squamous cell carcinoma patients when compared with long-term betel quid chewers, or compared with matched adjacent oral mucosa (Chiang et al., 2008).

3.2.2 P53

P53 is one of the most important tumor suppressor genes. Tumor suppressor genes work normally in cellular growth control by regulating the cell cycle, apoptosis, cell adhesion, and DNA repair. Silencing of tumor suppressor genes occurs in carcinogenesis. P53 mutation was also found to have an association with tobacco smoking and alcohol drinking. Inactivation of P53 by mutations is a critical molecular event in the upper aero-digestive tract carcinogenesis (Szymańska et al., 2010). Alteration of P53 expression is related to increased genomic instability in oral intraepithelial neoplasia and may accelerate the genetic modifications during oral tumorigenesis (Lippman et al., 2005). P53 codon72 polymorphism was found to be associated with a higher risk for contracting oral cancer (Kuroda et al., 2007).

3.2.3 Gene polymorphisms

Single nucleotide polymorphisms (SNPs) are genes areas that have altered DNA sequences which may not induce an aminoacid modification, or misrepresented DNA sequences that do not seem to have the potential for any unfavorable consequence in healthy people but may be markers for tendency to contract diseases (Scully & Petti, 2010). Certain genetic polymorphisms associated with enzymes for alcohol metabolism, such as, alcohol dehydrogenase genes and cytochrome P450 genes, are related to a greater risk of contracting oral squamous cell carcinoma. Besides, this risk is proportional to the amount of alcohol consumption (Marichalar-Mendia et al., 2010). Previous studies found hypoxia inducible factor-1 alpha gene polymorphisms C1722T and G1790A were associated with an increased risk of contracting oral cancer (Chen et al., 2009; Shieh et al., 2010). SNPs of the vascular endothelial growth factor gene were reported to have an association with development of oral cancer. The +936 T allele and the -2578 C/A SNP were expressed significantly more often in peripheral blood samples from oral squamous cell carcinoma patients when compared with those from healthy controls (Kämmerer et al., 2010). In a meta-analysis of case-control study, Arg194Trp polymorphism in the X-ray repair cross-complementing group 1 gene was significantly associated with oral cancer in an Asian population (Zhou et al., 2009).

3.2.4 Others

Promoter methylation of human MutL homolog1 (hMLH1) was found in 76% of oral squamous cell carcinoma patients but in none of the healthy control samples. The hMLH1 gene belongs to the human DNA mismatch repair system and is essential in reducing the accumulation of mutations and maintaining genomic stability (González-Ramírez et al., 2011).

3.3 Infectious factors

Infection can be induced by bacteria, fungus, and virus. Periodontal disease has been shown to increase the risk of oral cancer. This chronic infection and resultant low-grade systemic inflammatory response along with oxidative stress may be one possible pathway of carcinogenesis (Gasche et al., 2011). Also, the oral ecological shifts accompanying periodontal disease are characterized by proliferation of ketone-producing and nitrate-reducing microorganisms, which may contribute to increases in carcinogen concentrations (Divaris et al., 2010). Furthermore, several oral microorganisms can produce carcinogenic acetaldehyde from alcohol (Homann et al., 2000). This may explain why poor oral hygiene is associated with oral cancer. A case-control study conducted in Japan found that frequent toothbrushing could reduce the risk of upper aerodigestive tract cancer, especially in those who are heavy smokers and drinkers (Sato et al., 2011).

Candida albicans is the yeast most commonly isolated from the oral cavity. *Candida* may invade oral epithelium and may be causally involved in dysplastic change. Nitrosamines produced by *Candida* may activate specific proto-oncogens. *Candida* can also efficiently convert ethanol into carcinogenic acetaldehyde (Scully, 2011).

Presently, more than 100 types of human papilloma viruses (HPV) have been identified. HPV-16 and HPV-18 are the most common virus types identified in oral carcinoma. Two meta-analyses found HPV is an independent risk factor for oral and oropharyngeal carcinoma (Dayyani et al., 2010; Hobbs et al., 2006). Two proteins of HPV, E6 and E7, are thought to be involved in the carcinogenesis of oral cancer. The E6 protein can bind to the cellular P53 protein and this leads to the breakdown and reduction in concentration of P53 in the cancer cell. As a consequence, the damaged cancer cells lose their ability to repair DNA and cannot undergo apoptosis. The E7 protein has the ability to bind the cellular RB protein, releasing transcription factors, which are then free to transactivate the expression of other cellular proteins (Shillitoe, 2009). A previous study has showed a combination of herpes simplex virus seropositivity and a history of smoking was associated with a higher risk of oral cancer than would be expected from a purely additive effect (Starr et al., 2001), However, the nature of the herpes simplex virus genome makes it difficult to generate specific probes and the possible sequences that were detected have not been identified (Shillitoe, 2009).

3.4 Environmental factors

3.4.1 Sunlight

In Denmark, a population-based case-control study found that individuals who were employed in outdoor work for more than 10 years had a 1.67-fold (95% confidence interval 1.38 ~ 2.03) increased risk of contracting lip cancer (Kenborg et al., 2010). The lower lip receives more direct sunlight than the upper lip. Therefore, lip cancer tends to develop in lower lip. However, it is interesting to note that the basal cell cancer and cutaneous malignant melanoma were less prevalent in outdoor workers in aforementioned study.

3.4.2 Heavy metals

Heavy metals are extremely persistent in the environment and can induce unfavorable consequences on human body. Heavy metals are incorporated into food crops grown in the

soils, and subsequently find their way into the human body following the consumption of such contaminated food items. The IARC classifies many heavy metals, such as arsenic (As), chromium (Cr), and nickel (Ni), as human carcinogens (Chiang et al., 2010). In an observational study conducted in Taiwan, the incidence of oral cancer was geographically associated with the concentrations of As and Ni in the patients' residential areas (Su et al., 2010). Blood levels of Ni and Cr in oral cancer patients were 1.6 and 1.4 times higher, respectively, than those of healthy controls in a case-control study. Individuals with high Ni blood level had a 16-fold higher relative risk of contracting oral cancer than those with low Ni blood level. Also, people with high Cr blood level had a 7-fold higher relative risk of contracting oral cancer than those with low Cr blood level (Yuan et al., 2011). The role of heavy metals in the mechanism of development of oral cancer warrants further investigation.

3.5 Dietary factors

It is interesting to find that caffeinated coffee drinking was inversely related with the risk of oral cavity cancer (odds ratio: 0.96, 95% confidence interval: 0.94 ~ 0.98) in a pooled case-control study (Galeone et al., 2010). In addition, people who had a dietary pattern of animal product consumption had a greater risk of developing oral cancer (odds ratio: 1.56, 95% confidence interval: 1.13-2.15) (Edefonti et al., 2010). Moreover, women with low folate intake had a higher risk of developing oral cancer if they also consumed a high amount of alcohol (Shanmugham et al., 2010). On the other hand, a traditional Mediterranean diet was found to reduce the risk of upper aerodigestive tract cancers in a case-control study conducted in Greece (Samoli et al., 2010). Intake of citrus fruit was also reported to lower the risk of developing oral cancer (Foschi et al., 2010). Although some studies showed that the Mediterranean-type diet and vegetable rich diet could reduce the risk of oral cancer, the evidence is still weak. The effect of individual food components and trace elements on carcinogenesis remains unclear (Meurman, 2010).

3.6 Socio-economic factors

There was a significant increase in the incidence of head and neck cancer including oral cancer in people with low level of education (odds ratios: 1.85 ~ 5.3) and lower income patients (odds ratios: 1.7 ~ 2.41) (Boing et al., 2011; Conway et al., 2008; Johnson et al., 2010; Madani et al., 2010; Swaminathan et al., 2009). Although there was a strong association between smoking/alcohol consumption and socioeconomic status, individuals with lower education level, lower income, lower occupational status/social class, and those performing manual labor still had a higher risk of contracting head and neck cancer including oral cancer after adjusting for smoking and alcohol consumption (Boing et al., 2011; Conway et al., 2008). Possible explanations includes, limited access to health care and health information, exposure to harmful physical environments and agents, and stresses caused by job insecurity or unemployment, and so on (Conway et al., 2008).

3.7 Ethnicity and race

The incidence rates of oral cancer vary considerably across racial/ethnic groups worldwide (Warnakulasuriya, 2009a). South Asians have higher incidence rates of oral cancer than people from most other countries. Black males in the United States have higher rates of

oropharyngeal cancer than white males (Warnakulasuriya, 2009b). However, such results could be confounded by nutritional difference, smoking pattern, differences in the amounts of cigarettes smoked or alcohol consumed, and interaction among smoking, alcohol consumption, and betel quid chewing.

3.8 Others

A previous study about the development of secondary solid tumors after allogeneic hematopoietic bone marrow transplant in Japan found that the risk for developing oral cavity cancer among those who had received such a transplant was 35.25-fold (95% confidence interval: 17.59 ~ 63.06) higher than that of the age- and sex-adjusted general population (Yokota et al., 2011). Body mass index gain was inversely associated with upper aero-digestive tract cancers including oral cancer in a large scale, prospective, multi-center study in European countries. It was speculated that this phenomenon might be due to other confounding factors, including interactions of body fat distribution with smoking and/or drinking, biological mechanisms, indication of early tumor development or other related carcinogenic mechanisms (Lubin et al., 2010; Park et al., 2011). A retrospective study found a significant association between chronic trauma of oral mucosa and oral cancer after adjusting for confounding factors, such as smoking and alcohol consumption (Piemonte et al., 2010). Sexual behaviors, such as more frequent sexual partners and oral sex were also reported to be associated with increased risk of oral cancer (Heck et al., 2010). However, such results may be confounded by HPV infection status.

3.9 Controversial risk factors

Although some studies found that heredity/familial risk, marijuana (cannabis) smoking, khat (qat) chewing, nicotine replacement therapy, human immunodeficiency virus infection, and alcohol in mouthwashes were linked with higher risk of developing oral cancer, these results are controversial and further investigation is still needed to elucidate the relationship between aforementioned factors and oral cancer (Warnakulasuriya, 2009b).

4. Prevention of oral cancer

A majority of people are at greater risks of developing oral cancer as a result of exposure to tobacco and/or alcohol or betel quid. It is estimated that a billion men and 250 million women smoke cigarettes, 2 billion people consume alcohol, and 600-1,200 million people chew betel quid worldwide (Scully, 2011). Therefore, oral cancer is largely preventable by lifestyle modification. A previous study found at least three-quarters of oral cancers could be avoided by the elimination of unsafe lifestyles such as cigarette smoking and alcoholic consumption. Smoking cessation contributes to decreased risk of oral cancers, with 35% decrease in risk within 1-4 years and 80% decrease of risk by 20 years, reaching the level of those who have never smoked lifelong non-smokers (Marron et al., 2010).

The most frequently used screening method for oral cancer is visual and physical examination of oral mucosa. Many studies have demonstrated that such screening programs could detect potentially malignant and malignant lesions at very early stages. However, there is still not enough concrete evidence to conclude if screening alters disease-specific mortality in asymptomatic person seeking dental care (Rethman, et al., 2010).

Although the use of non-steroid anti-inflammatory drugs (NSAID) has been associated with a reduced risk of developing several types of cancer, no definite conclusion or consensus has been reached on the effect of NSAIDs on head and neck cancer risk. Further large-scale studies are mandatory to elucidate possible relationships between NSAIDs and head and neck cancer (Wilson et al., 2011).

5. Conclusion

Recognition of relevant risk factors for oral cancer can help physician to identify those patients at greater risk of developing oral cancer. Besides, it can help health authorities to implement effective programs to prevent oral cancer. Furthermore, it is important to educate the public about the relevant risk factors of contracting oral cancer so that those with unhealthy habits can modify their lifestyles.

6. References

Altieri, A. et al. (2004). Wine, beer and spirits and risk of oral and pharyngeal cancer: a case-control study from Italy and Switzerland. *Oral Oncology*, Vol.40, No.9, pp. 904-909, ISSN 1368-8375

Boing, AF. et al. (2011). How much do smoking and alcohol consumption explain socioeconomic inequalities in head and neck cancer risk? *Journal of Epidemiology and Community Health*, Vol.65, No.8, pp. 709-714, ISSN 0143-005X

Bunnell, A. et al. (2010). Analysis of primary risk factors for oral cancer from select US states with increasing rates. *Tobacco Induced Diseases,* Vol. 8, No. 1, pp. 5, ISSN 2070-7266

Castellsagué, X. et al. (2004). The role of type of tobacco and type of alcoholic beverage in oral carcinogenesis. *International Journal of Cancer,* Vol.108, No.5, pp. 741-749, ISSN 0020-7136

Chang, YC. et al. (2001). Synergistic effects of nicotine on arecoline-induced cytotoxicity in human buccal mucosal fibroblasts. *Journal of Oral Pathology & Medicine,* Vol. 30, No. 8, pp. 458-464, ISSN 0904-2512

Chen, MK. et al. (2009). The association between hypoxia inducible factor-1alpha gene polymorphisms and increased susceptibility to oral cancer. *Oral Oncology*, Vol.45, No.12, pp. e222-e226, ISSN 1368-8375

Chiang, CT. et al. (2010). Spatiotemporal trends in oral cancer mortality and potential risks associated with heavy metal content in Taiwan soil. *International Journal of Environmental Research and Public Health*, Vol.7, No.11, pp. 3916-3928, ISSN 1661-7827

Chiang, WF. et al. (2008). Association of epidermal growth factor receptor (EGFR) gene copy number amplification with neck lymph node metastasis in areca-associated oral carcinomas. *Oral Oncology,* Vol.44, No.3, pp. 270-276, ISSN 1368-8375

Conway, DI. et al. (2008). Socioeconomic inequalities and oral cancer risk: a systematic review and meta-analysis of case-control studies. International Journal of Cancer, Vol.122, No.12, pp. 2811-2819, ISSN 0020-7136

Dayyani, F. et al. (2010). Meta-analysis of the impact of human papillomavirus (HPV) on cancer risk and overall survival in head and neck squamous cell carcinomas (HNSCC). *Head & Neck Oncology*, Vol.2, pp.15, ISSN 1758-3284

Divaris, K. et al. (2010). Oral health and risk for head and neck squamous cell carcinoma: the Carolina Head and Neck Cancer Study. *Cancer Causes Control*, Vol.21, No.4, pp. 567-575, ISSN 0957-5243

Edefonti, V. et al. (2010). Nutrient-based dietary patterns and the risk of oral and pharyngeal cancer. Oral Oncology, Vol.46, No.5, pp. 343-348, ISSN 1368-8375

Ferlay, J. et al. (2010). Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *International Journal of Cancer,* Vol.127, No.12, pp. 2893–2917, ISSN 0020-7136

Foschi, R. et al. (2010). Citrus fruit and cancer risk in a network of case-control studies. *Cancer Causes Control*, Vol.21, No.2, pp. 237-242, ISSN 0957-5243

Galeone, C. et al. (2010). Coffee and tea intake and risk of head and neck cancer: pooled analysis in the international head and neck cancer epidemiology consortium. *Cancer Epidemiology, Biomarkers & Prevention*, Vol.19, No.7, pp. 1723-1736, ISSN 1055-9965

Garnis, C. et al. (2009). Genomic imbalances in precancerous tissues signal oral cancer risk. *Molecular cancer,* Vol.8, pp. 50, doi: 10.1186/1476-4598-8-50, ISSN 1476-4598

Gasche, JA. et al. (2011). Interleukin-6 promotes tumorigenesis by altering DNA methylation in oral cancer cells. *International Journal of Cancer*, Vol.129, No.5, pp. 1053-1063, ISSN 0020-7136

González-Ramírez, I. et al. (2011). hMLH1 promoter methylation is an early event in oral cancer. *Oral Oncology*, Vol.47, No.1, pp. 22-26, ISSN 1368-8375

Heck, JE. et al. (2010). Sexual behaviours and the risk of head and neck cancers: a pooled analysis in the International Head and Neck Cancer Epidemiology (INHANCE) consortium. *International Journal of Epidemiology*, Vol.39, No.1, pp. 166-181, ISSN 0300-5771

Hobbs, CG. et al. (2006). Human papillomavirus and head and neck cancer: a systematic review and meta-analysis. *Clinical Otolaryngology*, Vol.31, No.4, pp. 259-266, ISSN 1749-4478

Homann, N. et al. (2000). Increased salivary acetaldehyde levels in heavy drinkers and smokers: a microbiological approach to oral cavity cancer. *Carcinogenesis,* Vol.21, No.4, pp. 663-668, ISSN 0143-3334

Ihsan, R. et al. (2011). Investigation on the role of p53 codon 72 polymorphism and interactions with tobacco, betel quid, and alcohol in susceptibility to cancers in a high-risk population from North East India. *DNA and Cell Biology*, Vol.30, No.3, pp. 163-171, ISSN 1044-5498

Janmaat ML. & Giaccone G. (2003). Small-molecule epidermal growth factor receptor tyrosine kinase inhibitors. *The Oncologist*, Vol.8, No.6, pp. 576-86, ISSN 1083-7159

Jayalekshmi, PA. et al. (2011). Oral cavity cancer risk in relation to tobacco chewing and bidi smoking among men in Karunagappally, Kerala, India: Karunagappally cohort study. *Cancer Science,* Vol.102, No.2, pp. 460-467, ISSN 1347-9032

Johnson, S. et al. (2010). Socio-economic status and head and neck cancer incidence in Canada: a case-control study. *Oral Oncology*, Vol.46, No.3, pp. 200-203, ISSN 1368-8375

Kämmerer, PW. et al. (2010). Single nucleotide polymorphisms of the vascular endothelial growth factor gene associated with incidence of oral squamous cell carcinoma. *Journal of Oral Pathology & Medicine*, Vol.39, No.10, pp. 786-792, ISSN 0904-2512

Kenborg, L. et al. (2010). Occupational exposure to the sun and risk of skin and lip cancer among male wage earners in Denmark: a population-based case-control study. *Cancer Causes & Control,* Vol.21, No.8, pp. 1347-1355, ISSN 0957-5243

Ko, YC. et al. (1995). Betel quid chewing, cigarette smoking and alcohol consumption related to oral cancer in Taiwan. *Journal of Oral Pathology & Medicine,* Vol.24, No.10, pp. 450-453, ISSN 0904-2512

Kuroda, Y. et al. (2007). Association between the TP53 codon72 polymorphism and oral cancer risk and prognosis. *Oral Oncology*, Vol.43, No.10, pp. 1043-1048, ISSN 1368-8375

Lachenmeier, DW. & Monakhova, YB. (2011). Short-term salivary acetaldehyde increase due to direct exposure to alcoholic beverages as an additional cancer risk factor beyond ethanol metabolism. *Journal of experimental & clinical cancer research,* Vol.30, No.1, pp. 3, ISSN 0392-9078

Lee, YC. et al. (2009). Active and involuntary tobacco smoking and upper aerodigestive tract cancer risks in a multicenter case-control study. *Cancer epidemiology, biomarkers & prevention,* Vol.18, No.12, pp. 3353-3361, ISSN 1055-9965

Li, Y.; Yang, H. & Cao, J. (2011). Association between alcohol consumption and cancers in the Chinese population – A systematic review and meta-analysis. *PloS ONE,* Vol.6, No.4, pp. e18776, ISSN 1932-6203

Lippman, SM.; Sudbo, J. & Hong, WK. (2005) Oral cancer prevention and the evolution of molecular-targeted drug development. *Journal of Clinical Oncology*, Vol.23, No.2, pp. 346-356, ISSN 0732-183X

Liu, SA. et al. (2006). Nutritional factors and survival of oral cancer patients. *Head & Neck,* Vol.28, No.11, pp. 998-1007, ISSN 1043-3074

Lubin, JH. et al. (2009). Total exposure and exposure rate effects for alcohol and smoking and risk of head and neck cancer: a pooled analysis of case-control studies. *American Journal of Epidemiology,* Vol.170, No.8, pp. 937-947, ISSN 0002-9262

Lubin, JH. et al. (2010). Body mass index, cigarette smoking, and alcohol consumption and cancers of the oral cavity, pharynx, and larynx: modeling odds ratios in pooled case-control data. American Journal of Epidemiology, Vol.171, N0.12, pp. 1250-1261, ISSN 0002-9262

Madani, AH. et al. (2010). Relationship between Selected Socio-Demographic Factors and Cancer of Oral Cavity - A Case Control Study. *Cancer Informatics*, Vol.11, No.9, pp. 163-168, ISSN 1176-9351

Marichalar-Mendia, X. et al. (2010). Oral cancer and polymorphism of ethanol metabolising genes. *Oral Oncology*, Vol.46, No.1, pp. 9-13, ISSN 1368-8375

Marron, M. et al. (2010). Cessation of alcohol drinking, tobacco smoking and the reversal of head and neck cancer risk. *International Journal of Epidemiology,* Vol.39, No.1, pp. 182-196, ISSN 0300-5771

Meurman, JH. (2010). Infectious and dietary risk factors of oral cancer. Oral Oncology, Vol.46, No.6, pp. 411-413, ISSN 1368-8375

Park, SL. et al. (2011). The association between change in body mass index and upper aerodigestive tract cancers in the ARCAGE project: multicenter case-control study. *International Journal of Cancer*, Vol.128, No.6, pp. 1449-1461, ISSN 0020-7136

Patel, BP. et al. (2010). Mutagen sensitivity in oral cancer patients, healthy tobacco chewers and controls. *Acta cytologica,* Vol.54, No.2, pp. 169-174, ISSN 0001-5547

Piemonte, ED.; Lazos, JP. & Brunotto, M. (2010). Relationship between chronic trauma of the oral mucosa, oral potentially malignant disorders and oral cancer. *Journal of Oral Pathology & Medicine,* Vol.39, No.7, pp. 513-517, ISSN 0904-2512

Ramadas, K. et al. (2003) Interim results from a cluster-randomized, controlled oral cancer screening trial in Kerala, India. *Oral Oncology,* Vol.39, No.6, pp. 580-588, ISSN 1368-8375

Rethman, MP. et al. (2010). Evidence-based clinical recommendations regarding screening for oral squamous cell carcinomas. *Journal of American Dental Association,* Vol.141, No.5, pp. 509-520, ISSN 0002-8177

Reznick, AZ. et al. (2003). Inhibition of oral peroxidase activity by cigarette smoke: in vivo and in vitro studies. *Free Radical Biology & Medicine,* Vol. 34, No.3, pp. 377-384, ISSN 0891-5849

Rohrer, J.; Wuertz, BR. & Ondrey, F. (2010). Cigarette smoke condensate induces nuclear factor kappa-b activity and proangiogenic growth factors in aerodigestive cells. *Laryngoscope,* Vol. 120, No.8, pp. 1609-1613, ISSN 0023-852X

Samoli, E. et al. (2010). Mediterranean diet and upper aerodigestive tract cancer: the Greek segment of the Alcohol-Related Cancers and Genetic Susceptibility in Europe study. *The British Journal of Nutrition*, Vol.104, No.9, pp. 1369-1374, ISSN 0007-1145

Sato, F. et al. (2011). Inverse association between toothbrushing and upper aerodigestive tract cancer risk in a japanese population. *Head & Neck*, Jan 21. doi: 10.1002/hed.21649. (Epub ahead of print), ISSN 1043-3074

Scully C. Oral cancer aetiopathogenesis; past, present and future aspects. (2011). *Medicina Oral, Patología Oral y Cirugía Bucal,* Vol.16, No.3, pp. e306-11 ISSN 1698-4447

Scully, C. & Petti, S. (2010) Overview of cancer for the healthcare team: Aetiopathogenesis and early diagnosis. Oral Oncology, Vol.46, No.6, pp.402-406, ISSN 1368-8375

Shanmugham, JR. et al. (2010). Alcohol-folate interactions in the risk of oral cancer in women: a prospective cohort study. *Cancer Epidemiology, Biomarkers & Prevention,* Vol.19, No.10, pp. 2516-2524, ISSN 1055-9965

Shieh, TM. et al. (2010). Association between the polymorphisms in exon 12 of hypoxia-inducible factor-1alpha and the clinicopathological features of oral squamous cell carcinoma. *Oral Oncology*, Vol.46, No.9, pp. e47-e53, ISSN 1368-8375

Shillitoe, EJ. (2009). The role of viruses in squamous cell carcinoma of the oropharyngeal mucosa. *Oral Oncology*, Vol.45, No.4-5, pp. 351-355, ISSN 1368-8375

Smith, EM. et al. (2010). Tobacco and alcohol use increases the risk of both HPV-associated and HPV-independent head and neck cancers. *Cancer Causes & Control,* Vol.21, No.9, pp. 1369-1378, ISSN 0957-5243

Starr, JR. et al. (2001). Serologic evidence of herpes simplex virus 1 infection and oropharyngeal cancer risk. *Cancer Research*, Vol.61, No.23, pp. 8459-8464, ISSN 0008-5472

Su, CC. et al. (2010). Incidence of oral cancer in relation to nickel and arsenic concentrations in farm soils of patients' residential areas in Taiwan. *BMC public health*, Vol.10, pp. 67, ISSN 1471-2458

Swaminathan, R. et al. (2009). Education and cancer incidence in a rural population in south India. *Cancer Epidemiology*, Vol.33, N0.2, pp. 89-93, ISSN 1877-7821

Szymańska, K. et al. (2010). TP53 and EGFR mutations in combination with lifestyle risk factors in tumours of the upper aerodigestive tract from South America. *Carcinogenesis*, Vol.31, No.6, pp. 1054-1059, ISSN 0143-3334

Szymańska, K. et al. (2011). Alcohol and tobacco, and the risk of cancers of the upper aerodigestive tract in Latin America: a case-control study. *Cancer Causes & Control,* Vol.22, No.7, pp. 1037-1046, ISSN 0957-5243

Takács, D. et al. (2011). Decreased oral cancer risk by moderate alcohol consumption in non-smoker postmenopausal women. *Oral Oncology,* Vol.47, No.6, pp. 537-540, ISSN 1368-8375

Taoudi Benchekroun, M. et al. (2010). Epidermal growth factor receptor expression and gene copy number in the risk of oral cancer. *Cancer prevention research (Philadelphia, Pa.),* Vol.3, No.7, pp. 800-809, ISSN 1940-6207

Tsai, KY. et al. (2009) Quantification of betel quid chewing and cigarette smoking in oral cancer patients. *Community Dentistry and Oral Epidemiology,* Vol.37, No.6, pp. 555-561, ISSN 0301-5661

Tsai, YS. et al. (2008). Arecoline, a major alkaloid of areca nut, inhibits p53, represses DNA repair, and triggers DNA damage response in human epithelial cells. *Toxicology*, Vol.249, No.2-3, pp. 230-237, ISSN 0300-483X

Warnakulasuriya, S. (2009a). Global epidemiology of oral and oropharyngeal cancer. *Oral Oncology*, Vol.45, No.4-5, pp. 309-316, ISSN 1368-8375

Warnakulasuriya, S. (2009b). Causes of oral cancer – an appraisal of controversies. *British Dental Journal,* Vol.207, No.10, pp. 471-475, ISSN 0007-0610

Wen, CP. et al. (2010). Cancer risks from betel quid chewing beyond oral cancer: a multiple-site carcinogen when acting with smoking. *Cancer Causes & Control,* Vol.21, No.9, pp. 1427-1435, ISSN 0957-5243

Wilson, JC. et al. (2011). Non-steroidal anti-inflammatory drug and aspirin use and the risk of head and neck cancer: a systemic review. *Cancer Causes & Control,* Vol.22, No.5, pp. 803-810, ISSN 0957-5243

Yen, TT. et al. (2008). The association of smoking, alcoholic consumption, betel quid chewing and oral cavity cancer: a cohort study. *European Archives of Otorhinolaryngology,* Vol.265, No.11, pp. 1403-1407, ISSN 0937-4477

Yokota, A. et al. (2011). Secondary solid tumors after allegeneic hematopoietic SCT in Japan. *Bone Marrow Transplantation,* Feb 28. (Epub ahead of print) doi:10.1038/bmt.2011.23, ISSN 0268-3369

Yuan, TH. et al. (2011). Possible association between nickel and chromium and oral cancer: a case-control study in central Taiwan. *Science of the Total Environment*, Vol.409, No.6, pp. 1046-1052, ISSN 0048-9697

Zhou, C. et al. (2009). The Arg194Trp polymorphism in the X-ray repair cross-complementing group 1 gene as a potential risk factor of oral cancer: a meta-analysis. *The Tohoku Journal of Experimental Medicine*, Vol.219, No.1, pp. 43-51, ISSN 0040-8727
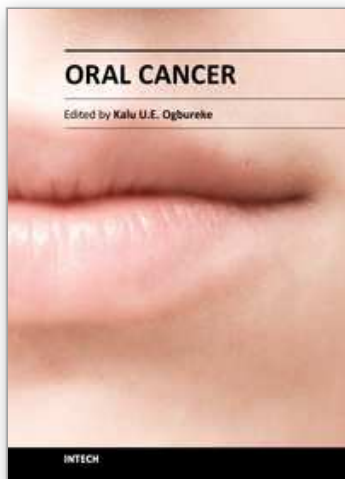
Oral Cancer

Edited by Dr. Kalu U. E. Ogbureke

ISBN 978-953-51-0228-1

Hard cover, 388 pages

Publisher InTech

Published online 14, March, 2012

Published in print edition March, 2012

Oral cancer is a significant public health challenge globally. Although the oral cavity is easily accessible, early diagnosis remains slow compared to the enhanced detection of cancers of the breast, colon, prostate, and melanoma. As a result, the mortality rate from oral cancer for the past four decades has remained high at over 50% in spite of advances in treatment modalities. This contrasts with considerable decrease in mortality rates for cancers of the breast, colon, prostate, and melanoma during the same period. This book attempts to provide a reference-friendly update on the etiologic/risk factors, current clinical diagnostic tools, management philosophies, molecular biomarkers, and progression indicators of oral cancer.

INTECH
open science | open minds