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Oral Cancer: Risk Factors, Diet and causes

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Abstract

Oral cancer is a significant global health concern, posing a substantial threat to public health due to its increasing incidence and often late diagnosis. This review article explores the key aspects of oral cancer, emphasizing its prevalence, risk factors, clinical presentation, diagnosis, and treatment options. Tobacco and alcohol consumption remain the primary risk factors, while emerging evidence highlights the role of HPV infection, poor oral hygiene, and genetic predisposition. Early symptoms such as persistent mouth sores, unexplained pain, and difficulty swallowing are often overlooked, leading to delayed diagnosis and reduced survival rates. Effective diagnosis relies on clinical examinations, imaging techniques, and biopsies, while advancements in molecular diagnostics offer promising tools for early detection. Treatment options, including surgery, radiation, chemotherapy, and targeted therapies, continue to evolve, improving patient outcomes. Additionally, ongoing research in immunotherapy and personalized medicine is paving the way for innovative treatment strategies. Raising public awareness, encouraging preventive measures, and supporting research initiatives are vital in reducing the global burden of oral cancer. This review aims to provide a comprehensive understanding of oral cancer, highlighting the importance of early detection, improved treatment strategies, and future research directions.

Keywords: Oral cancer; Risk factors; Early detection; Diagnosis; Treatment strategies; Public awareness

1. Introduction

Oral cancer is a significant global health concern, affecting millions of people each year. It refers to malignant tumors that develop in the oral cavity, including the lips, tongue, gums, inner cheeks, floor of the mouth, hard and soft palate, and pharynx. The most common type is squamous cell carcinoma, which accounts for over 90% of all oral cancer cases. Like other cancers, oral cancer can spread to nearby tissues and distant organs if not detected and treated early, making early diagnosis crucial for better outcomes.

The importance of studying for oral cancer cannot be overstated. It remains a leading cause of cancer-related morbidity and mortality worldwide, often diagnosed at an advanced stage due to the lack of early symptoms and awareness. The disease significantly impacts an individual's quality of life, affecting speech,

chewing, swallowing, and even facial aesthetics. Beyond the personal level, oral cancer places a substantial burden on healthcare systems, particularly in low- and middle-income countries where access to medical care and awareness programs may be limited.

Epidemiologically, oral cancer shows a highly variable prevalence across different regions. Globally, it ranks among the top 15 most common cancers, with a particularly high incidence in South and Southeast Asia, parts of Europe, and South America. India, for example, reports some of the highest oral cancer rates, largely attributed to the widespread use of tobacco and areca nut products. In Western countries, lifestyle factors such as alcohol consumption, smoking, and human papillomavirus (HPV) infection are major contributors. Despite advances in treatment, the five-year survival rate for oral cancer remains relatively low, emphasizing the need for better preventive and diagnostic measures.

The objective of this review is to provide a comprehensive understanding of oral cancer by exploring its risk factors, pathophysiology, diagnosis, treatment options, and prevention strategies. By consolidating recent research and epidemiological data, this article aims to highlight the current challenges in managing oral cancer while emphasizing the importance of early detection and public awareness. Ultimately, this review seeks to contribute to the ongoing efforts in reducing the burden of oral cancer globally and improving patient outcomes through enhanced preventive and therapeutic approaches.

2. Risk Factors for Oral Cancer

Oral cancer is a complex disease influenced by a variety of risk factors, both lifestyle-related and genetic. Understanding these factors is crucial in preventing and managing the disease effectively. While some of these risks are well-established, others are still being studied for their potential role in oral cancer development. Here's a closer look at the major risk factors contributing to oral cancer.

2.1. Tobacco Use (Smoking and Smokeless Tobacco)

Tobacco consumption is the leading cause of oral cancer, accounting for a significant number of cases worldwide. Both smoking and smokeless forms of tobacco, such as chewing tobacco, betel quid, and snuff, expose the mouth to carcinogenic chemicals that damage the cells lining the oral cavity. Cigarettes, cigars, and pipes increase the risk of malignant changes, while smokeless tobacco products, commonly used in South and Southeast Asia, are particularly harmful as they are in direct contact with oral tissues for prolonged periods. Research suggests that long-term tobacco users have a 5 to 10 times higher risk of developing oral cancer than non-users.

2.2. Alcohol Consumption

Excessive alcohol consumption is another significant risk factor for oral cancer. Alcohol can irritate and damage the mucosal lining of the mouth, making it more susceptible to carcinogenic changes. Moreover, alcohol acts synergistically with tobacco, meaning individuals who consume both have a dramatically higher risk of developing oral cancer compared to those who use either substance alone. Studies indicate that heavy alcohol drinkers are at least twice as likely to develop oral cancer as non-drinkers. The risk increases with the frequency and duration of alcohol consumption, especially when combined with poor dietary habits.

2.3. Human Papillomavirus (HPV) Infection

In recent years, human papillomavirus (HPV) infection, particularly HPV-16, has emerged as a significant risk factor for oral and oropharyngeal cancers. HPV is a sexually transmitted virus that can infect the mucosal

surfaces of the mouth and throat. Unlike traditional risk factors such as tobacco and alcohol, HPV-related oral cancers tend to affect younger individuals who may not have a history of smoking or drinking. HPV-positive oral cancers generally have a better prognosis than HPV-negative ones, but increasing awareness about HPV vaccination and safe practices remains essential in reducing this risk.

2.4. Other Factors: Diet, Genetics, and Oral Hygiene

A poor diet lacking essential vitamins and minerals can contribute to the development of oral cancer. Diets low in fruits and vegetables, which provide antioxidants and protective nutrients, may increase susceptibility to cancer. Certain genetic mutations and a family history of oral cancer can also predispose individuals to the disease, though environmental factors often play a more dominant role.

Poor oral hygiene and chronic irritation from ill-fitting dentures, sharp teeth, or persistent infections can also contribute to oral cancer risk. Long-term exposure to these irritants may lead to chronic inflammation, increasing the likelihood of malignant transformation in oral tissues.

2.5. Socioeconomic Factors

Socioeconomic status plays an indirect but crucial role in oral cancer risk. People from lower-income backgrounds may have limited access to healthcare, leading to delayed diagnoses and poorer outcomes. Additionally, higher tobacco and alcohol consumption rates, lack of awareness about oral cancer, and inadequate access to nutritious food further increase the risk in economically disadvantaged populations.

3. Symptoms and Clinical Presentation of Oral Cancer

Oral cancer often develops silently, with symptoms that may initially seem harmless. This makes early detection challenging, leading to delayed diagnosis and poorer treatment outcomes. Understanding the warning signs and how oral cancer progresses is essential for timely intervention and better survival rates.

3.1. Common Symptoms

Oral cancer can manifest in various ways, depending on its location and stage. Some of the most common symptoms include:

- **Persistent Mouth Ulcers or Sores:** Unlike typical mouth ulcers, cancerous lesions do not heal within two weeks and may bleed easily.
- **Red or White Patches:** Leukoplakia (white patches) and erythroplakia (red patches) in the mouth can indicate precancerous or cancerous changes.
- **Pain or Numbness:** Unexplained pain, tenderness, or numbness in the mouth, lips, or tongue can be a warning sign of malignancy.
- **Difficulty Swallowing or Chewing:** As the tumor grows, it can cause discomfort or a sensation of something being stuck in the throat.
- **Lump or Thickening in the Mouth or Neck:** A persistent lump, swelling, or thickened area in the mouth, jaw, or neck should not be ignored.
- **Changes in Voice or Speech Difficulties:** Tumors affecting the tongue or throat can lead to slurred speech or voice changes.
- **Loose Teeth or Jaw Pain:** If teeth become loose without any dental cause, it may be due to underlying cancer affecting the jawbone.

Since many of these symptoms can resemble other oral conditions, such as infections or benign ulcers, people often dismiss them, leading to a delay in seeking medical attention.

3.2. Staging of Oral Cancer

Oral cancer is staged based on tumor size, lymph node involvement, and metastasis (spread to distant organs), classified as follows:

- Stage 0 (Carcinoma in Situ): Abnormal cells are present but have not invaded deeper tissues.
- Stage I & II: Early-stage cancer, where the tumor is relatively small (less than 4 cm) and has not spread to lymph nodes.
- Stage III: A larger tumor or cancer that has spread to nearby lymph nodes.
- Stage IV: Advanced cancer that may have spread to distant lymph nodes or other parts of the body, making treatment more complex.

3.3. Importance of Early Detection

Early detection is the key to improving survival rates and treatment success. When diagnosed at an early stage, oral cancer has a significantly higher chance of being treated successfully with surgery, radiation, or chemotherapy. Unfortunately, many cases are diagnosed in later stages when treatment options become more aggressive and less effective.

Regular dental check-ups, self-examinations, and awareness of persistent oral changes can help catch oral cancer in its early stages. Healthcare professionals play a crucial role in educating individuals about risk factors and screening programs, which can lead to earlier detection and improved patient outcomes.

By paying attention to early warning signs and seeking prompt medical advice, individuals can greatly reduce the impact of oral cancer, improving both survival rates and quality of life.

4. Diagnosis of Oral Cancer

Diagnosing oral cancer accurately and at an early stage is crucial for effective treatment and better patient outcomes. Since oral cancer often presents with subtle symptoms in its early stages, a combination of clinical examination, imaging techniques, and laboratory tests is necessary to confirm the presence of malignancy. Here's a closer look at the key diagnostic methods used to detect oral cancer.

4.1. Clinical Examination

The first step in diagnosing oral cancer is a thorough clinical examination conducted by a dentist, oral surgeon, or oncologist. This involves inspecting the oral cavity, tongue, gums, inner cheeks, and throat for abnormalities such as persistent ulcers, red or white patches, lumps, or swelling. The doctor may also palpate (feel) the neck and jaw area to check for enlarged lymph nodes, which can indicate cancer spread.

Patients with persistent symptoms like pain, difficulty swallowing, or unexplained bleeding should seek medical attention promptly. Regular dental check-ups play a vital role in early detection, as dentists can identify suspicious lesions before they become more advanced.

4.2. Imaging Techniques

Once a suspicious lesion is detected, imaging tests help assess the tumor's size, depth, and possible spread to nearby tissues or distant organs. Common imaging techniques include:

- X-rays: Used primarily to detect bone involvement, particularly in cases where oral cancer affects the jawbone.
- Computed Tomography (CT) Scan: Provides detailed cross-sectional images of the oral cavity, throat, and surrounding tissues. CT scans help determine if cancer has spread to nearby structures or lymph nodes.
- Magnetic Resonance Imaging (MRI): Offers high-resolution images of soft tissues, making it useful for evaluating tumor extent and nerve involvement.
- Positron Emission Tomography (PET) Scan: Often combined with CT scans, PET scans help identify cancer spread to distant parts of the body by detecting increased metabolic activity in cancerous cells.

Each of these imaging techniques plays a role in staging the disease and planning an appropriate treatment strategy.

4.3. Biopsy and Histopathological Examination

A definitive diagnosis of oral cancer requires a biopsy, in which a small tissue sample is taken from the suspicious lesion for further analysis. There are different types of biopsies used in oral cancer diagnosis:

- Incisional Biopsy: A small part of the lesion is removed for examination, typically used for larger or deeper tumors.
- Excisional Biopsy: The entire lesion is removed, often performed for small, localized growths.
- Fine Needle Aspiration (FNA): Used to extract cells from lymph nodes or suspected metastatic sites.

The collected tissue sample is then examined under a microscope by a pathologist in a process called histopathological examination. This helps determine whether the cells are cancerous, the type of cancer, and its grade (aggressiveness).

4.4. Role of Molecular Diagnostics

With advancements in cancer research, molecular diagnostics is becoming an essential tool in detecting and understanding oral cancer at a genetic level. These tests help identify specific genetic mutations, biomarkers, and molecular alterations in cancerous tissues. Some of the key molecular diagnostic techniques include:

- HPV Testing: Since human papillomavirus (HPV) is linked to certain types of oral cancer, detecting HPV DNA in biopsy samples can provide crucial insights into the nature of the cancer.
- Fluorescence in Situ Hybridization (FISH): Helps detect genetic abnormalities in cancer cells.
- Liquid Biopsy: A non-invasive test that analyzes cancer-related genetic material in the bloodstream, potentially allowing for early detection and monitoring of treatment response.

Molecular diagnostics not only aid in early detection but also help in selecting targeted therapies for personalized treatment plans.

5. Treatment Options for Oral Cancer

The treatment of oral cancer depends on several factors, including the stage of the disease, the tumor's location, and the patient's overall health. A combination of different treatment approaches is often required to achieve the best possible outcome. Advances in medical science have improved survival rates and quality of life for oral cancer patients, but early detection remains key to successful treatment. Here's an overview of the main treatment options available.

5.1. Surgical Interventions

Surgery is often the first-line treatment for oral cancer, particularly in its early stages. The goal of surgical intervention is to remove the tumor while preserving as much function of the mouth as possible. The type of surgery performed depends on the size and location of the tumor:

- **Tumor Resection:** The primary surgery involves removing the cancerous growth along with a margin of healthy tissue to ensure complete removal.
- **Glossectomy:** If the tumor affects the tongue, a partial or total removal of the tongue (glossectomy) may be necessary.
- **Mandibulectomy or Maxillectomy:** If the cancer has spread to the jawbone or upper palate, portions of the affected bone may need to be removed.
- **Neck Dissection:** Since oral cancer often spreads to nearby lymph nodes, a surgical procedure called neck dissection may be performed to remove affected lymph nodes and reduce the risk of recurrence.
- **Reconstructive Surgery:** After tumor removal, reconstructive procedures using grafts and prosthetics help restore speech, chewing, and facial aesthetics. Speech therapy and rehabilitation may also be needed post-surgery.

While surgery is often effective in eliminating cancer, it can have significant side effects, including difficulties with speech and swallowing. However, advancements in surgical techniques and post-operative care have improved recovery outcomes.

5.2. Radiation Therapy

Radiation therapy uses high-energy X-rays or other radiation particles to destroy cancer cells. It can be used alone in early-stage cancers or combined with surgery and chemotherapy in more advanced cases. There are two main types of radiation therapy:

- **External Beam Radiation Therapy (EBRT):** This is the most common form of radiation therapy, where targeted radiation is directed at the tumor from an external machine.
- **Brachytherapy:** In this approach, radioactive materials are placed directly inside or near the tumor site, providing localized treatment.

Radiation therapy is particularly effective in preventing cancer recurrence, but it can have side effects such as dry mouth, difficulty swallowing, and changes in taste. Newer techniques like intensity-modulated radiation therapy (IMRT) help minimize damage to surrounding healthy tissues.

5.3. Chemotherapy

Chemotherapy involves the use of powerful drugs to kill cancer cells or slow their growth. It is typically used in combination with radiation therapy (chemoradiation) for advanced-stage oral cancers or in cases where the cancer has spread to other parts of the body. Common chemotherapy drugs for oral cancer include cisplatin, fluorouracil (5-FU), and paclitaxel.

While chemotherapy can be effective, it often comes with side effects such as nausea, fatigue, hair loss, and a weakened immune system. Supportive care measures help patients manage these side effects during treatment.

5.4. Targeted Therapy and Immunotherapy

Advancements in cancer research have led to the development of targeted therapies and immunotherapies, which offer more personalized treatment approaches.

- **Targeted Therapy:** Unlike chemotherapy, targeted therapy drugs specifically attack cancer cells while minimizing damage to normal cells. One such drug is cetuximab, which targets the epidermal growth factor receptor (EGFR), a protein involved in cancer cell growth.
- **Immunotherapy:** This approach helps the body's immune system recognize and attack cancer cells. Immune checkpoint inhibitors such as pembrolizumab and nivolumab have shown promise in treating advanced oral cancers, particularly in patients who do not respond well to chemotherapy.

These newer treatments are revolutionizing cancer care, offering hope for improved survival rates with fewer side effects compared to traditional therapies.

5.5. Palliative Care

For patients with advanced or terminal oral cancer, palliative care plays a crucial role in improving quality of life. The focus is on managing pain, reducing symptoms, and providing emotional and psychological support to patients and their families. Palliative care may include:

- Pain management through medication or nerve blocks
- Nutritional support for patients with difficulty eating or swallowing
- Speech and swallowing therapy
- Emotional and psychological counseling

Palliative care can be provided alongside curative treatments or as end-of-life care when treatment is no longer effective. The goal is to ensure comfort and dignity for patients throughout their journey.

6. Prognosis and Survival Rates of Oral Cancer

The prognosis of oral cancer varies widely depending on several factors, including the stage at diagnosis, treatment received, and the patient's overall health. While advances in medical treatment have improved survival rates, early detection remains the most crucial factor in achieving a favorable outcome.

6.1. Factors Influencing Prognosis

Several key factors determine the prognosis of oral cancer:

- **Stage at Diagnosis:** The most significant factor influencing survival is the stage at which the cancer is diagnosed. Patients diagnosed at an early stage (Stages I and II) have a much better prognosis compared to those diagnosed at an advanced stage (Stages III and IV).
- **Tumor Size and Location:** Cancers that are small and localized have a better prognosis than those that have spread to lymph nodes or distant organs. Tumors affecting the tongue or the floor of the mouth tend to be more aggressive.
- **Lymph Node Involvement:** If the cancer has spread to nearby lymph nodes, the risk of recurrence increases, leading to a poorer prognosis.
- **HPV Status:** Human papillomavirus (HPV)-related oral cancers, particularly those affecting the oropharynx, generally have a better prognosis than HPV-negative cancers.
- **Patient's Overall Health:** Factors such as age, immune system function, and underlying health conditions can impact treatment success and recovery.
- **Lifestyle Choices:** Continued use of tobacco and alcohol after treatment significantly increases the risk of recurrence and negatively affects survival rates.

6.2. Survival Statistics Based on Stage and Treatment

Survival rates for oral cancer are typically measured in terms of the five-year survival rate, which indicates the percentage of patients who live at least five years after diagnosis. According to global cancer research data:

- **Stage I and II (Localized Cancer):** The five-year survival rate is around 70-80%, meaning that the majority of patients with early-stage oral cancer can expect a good outcome with appropriate treatment.
- **Stage III (Locally Advanced Cancer):** When the cancer has spread to nearby tissues or lymph nodes, the survival rate drops to around 50-60%.
- **Stage IV (Metastatic Cancer):** In cases where the cancer has spread to distant organs, the five-year survival rate is significantly lower, ranging between 20-30%.

Patients who undergo a combination of surgery, radiation, and chemotherapy have better chances of survival, especially if treatment is started early. However, recurrence remains a concern, particularly for those with advanced-stage cancer.

6.3. Importance of Follow-Up Care

Even after successful treatment, regular follow-up care is essential to monitor for recurrence and manage any long-term side effects. Follow-up visits typically include:

- Routine clinical examinations and imaging tests to check for signs of recurrence.
- Rehabilitation and supportive care to address speech, swallowing, and nutritional challenges after surgery or radiation.
- Counseling and lifestyle modifications to help patients quit smoking and reduce alcohol consumption, which are crucial in preventing recurrence.

Survivors of oral cancer need long-term monitoring, as the risk of developing a second primary tumor is higher compared to the general population. Early detection of recurrence or new malignancies through follow-up care can make a significant difference in survival outcomes.

6.4. Future Directions in Oral Cancer Research

The field of oral cancer research is rapidly evolving, with new advancements offering hope for better detection, treatment, and survival outcomes. Scientists and healthcare professionals are working toward more effective therapies, early diagnostic tools, and personalized treatment approaches that could revolutionize how we manage oral cancer. Here are some of the key areas shaping the future of oral cancer research.

6.5. Emerging Therapies and Clinical Trials

Traditional treatments like surgery, radiation, and chemotherapy have been the mainstay of oral cancer management for decades. However, new therapies are being developed to target cancer cells more precisely while minimizing damage to healthy tissues.

- **Immunotherapy:** Drugs like immune checkpoint inhibitors (e.g., pembrolizumab, nivolumab) are being studied to help the body's immune system recognize and destroy cancer cells. Immunotherapy has shown promising results, especially for patients with advanced or recurrent oral cancer.
- **Targeted Therapy:** Researchers are developing drugs that target specific genetic mutations and molecular pathways involved in cancer growth. For example, EGFR inhibitors (such as cetuximab) are already being used in some cases, and ongoing clinical trials aim to find new, more effective targets.
- **Gene Therapy:** Scientists are exploring ways to modify or repair genetic defects that contribute to oral cancer, potentially offering a long-term cure.

Participation in clinical trials is critical for testing these new therapies and improving current treatment protocols. Patients with oral cancer are encouraged to explore clinical trial opportunities, as these studies often provide access to cutting-edge treatments that are not yet widely available.

6.6. Role of Personalized Medicine

One of the most exciting developments in cancer treatment is the shift toward personalized medicine—tailoring therapies based on a patient's genetic profile, tumor characteristics, and overall health. Instead of a "one-size-fits-all" approach, personalized medicine uses:

- **Genomic Profiling:** Identifying specific genetic mutations in a patient's tumor can help doctors choose targeted therapies that are more likely to be effective.
- **Biomarkers for Treatment Response:** Researchers are working on identifying biomarkers that can predict how a patient will respond to a particular treatment, reducing unnecessary side effects and improving outcomes.
- **AI and Machine Learning:** Artificial intelligence is being used to analyze patient data and predict treatment responses, further advancing the precision of personalized cancer care.

As research progresses, personalized medicine has the potential to significantly improve survival rates and reduce the toxic side effects associated with conventional cancer treatments.

6.7. Advances in Early Detection Methods

Early detection remains the most crucial factor in improving oral cancer outcomes. New research is focused on developing non-invasive, highly sensitive diagnostic tools that can identify cancer at its earliest stages.

- **Saliva and Blood-Based Biomarkers:** Researchers are investigating specific molecules in saliva and blood that may indicate the presence of oral cancer before visible symptoms appear. These "liquid biopsies" could offer a simple and painless way to screen for cancer.
- **AI-Assisted Imaging:** Advanced imaging techniques, combined with artificial intelligence, are being developed to analyze oral lesions with high accuracy, helping dentists and doctors detect cancerous changes earlier.
- **Portable Screening Devices:** Efforts are being made to develop affordable, easy-to-use screening devices that can be used in remote or low-resource settings, improving access to early diagnosis worldwide.

With these advancements, the future of oral cancer detection looks promising, making it easier to diagnose the disease before it reaches an advanced stage.

7. Conclusion

Oral cancer remains a significant global health challenge, affecting thousands of people each year. Throughout this review, we have explored the various aspects of oral cancer, including its risk factors, symptoms, diagnosis, treatment options, prognosis, and future research directions. Early detection plays a crucial role in improving survival rates, as treatment is most effective when the disease is diagnosed at an early stage. Advances in medical research, including targeted therapies, immunotherapy, and personalized medicine, are paving the way for better treatment outcomes and improved quality of life for patients.

Despite these advancements, prevention remains the most effective way to reduce the burden of oral cancer. Raising awareness about key risk factors—such as tobacco use, excessive alcohol consumption, poor oral hygiene, and HPV infection—can help individuals make informed lifestyle choices that lower their risk of developing the disease. Regular dental check-ups, self-examinations, and early medical intervention for suspicious symptoms are essential steps in early detection.

Looking ahead, continued research and innovation are vital for improving oral cancer treatment and survival rates. Investment in new diagnostic technologies, increased participation in clinical trials, and public health initiatives focused on education and prevention are all critical. Governments, healthcare organizations, and communities must work together to promote screening programs and make treatment more accessible, especially in underserved areas.

By spreading awareness, supporting research, and advocating for early detection programs, we can take meaningful steps toward reducing the impact of oral cancer worldwide. It is a collective effort—one that requires the involvement of researchers, healthcare professionals, policymakers, and individuals alike. The fight against oral cancer is ongoing, but with continued dedication, progress is within reach.

Declaration of Conflicting Interests

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