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SQUAMOUS CELL CARCINOMA – OVERVIEW

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ABSTRACT

Squamous cell carcinoma (SCC) is 2 nd most common skin cancer in the world. It occurs mostly in anatomical locations like the head, chest, belly area, pelvis, and front and back of the body. Cutaneous squamous cell carcinoma (CSCC) damage is caused by sun exposure, which is known as actinic keratoses. Actinic means sun rays, and keratoses means roughly scaly skin patches on the skin. They cause serious harm in some cases, but they don't spread very quickly. Actinic keratoses are mostly caused by factors like scars, chronic radiation, and heat on the mucosal surface. Squamous cell carcinoma (SCC) is a type of nonmelanoma skin cancer that is common in Europe and Asia and is referred to as Caucasian. Factors that can increase the risk of squamous cell carcinoma (SCC) are excessive sun exposure, fair skin, sunburn, exposure to radiation. Therapies used to cure squamous cell carcinoma (SCC) head and neck are locally advanced (AV) and include surgical methods, that are radiotherapy (RT) and concurrent chemotherapy (CT). Radiotherapy (RT) and concurrent chemotherapy (CT). Radiotherapy is one of the most advanced and highly precise techniques used for the treatment of tumors. Studies for Squamous cell carcinoma head and neck, antibodies like cetuximab combined with platinum-based concurrent chemotherapy. Cetuximab is an antibody that targets and binds to epidermal growth factor receptor (EGFR) to inhibit the growth of tumor cells.

KEYWORDS: Anatomic location, Cutaneous squamous cell carcinoma (SCC), Actinic keratoses, Nonmelanoma skin cancer, Caucasians, Locally advanced, Radiotherapy (RT), Concurrent chemotherapy (CT), Cetuximab, Epidermal growth factor receptors.

INTRODUCTION

Nonmelanoma skin cancer (NMSK) is most common in Europe and Asia, which is referred to as Caucasians. Basal cell carcinoma (BCC) accounts for 75% of locally epidermal tumors with a metastatic rate of <0.1%. Cutaneous squamous cell carcinoma (CSCC) accounts for the majority of non-melanoma skin cancer, which arises from epidermal keratinocytes, the majority of which occur in a subgroup of high-risk in squamous cell carcinoma (SCC).[1] Several risk factors have been reported, which include Fitzpatrick skin type I and II.

Actinic keratoses are one of the significant factors in squamous cell carcinoma (SCC). Actinic keratoses are caused by harmful sun rays on rough, scaly skin patches on the skin. Actinic keratoses can cause serious harm in some cases, but they don't spread very quickly. Actinic keratoses range in size from 1 to 2 mm to large plaques, flesh-coloured or deeply pigmented. Although it is usually diagnosed on the basis of its appearance, it may be difficult or impossible to spot squamous cell carcinoma(SCC).[2] Actinic keratoses are mostly caused by factors like scars, chronic radiation, and heat on the mucosal surface. Factors that can increase the risk of squamous cell carcinoma (SCC) are excessive sun exposure, fair skin, sunburn, and exposure to radiation. It demonstrated that the p53 chromosomal mutation, found in 90% of human cutaneous squamous cell carcinoma(CSCC) present in actinic keratosis.[3,4] Estimates the percentage of chromosomal abnormal skin lesions that convert squamous cell carcinoma (SCC) rate increases from 0.25% to 20% per year. Patients often have multiple actinic keratoses, which are caused by the effects of solar and UV radiation, and most actinic keratoses and squamous cell carcinoma (SCC) are asymptomatic.[5] Human papillomavirus (HPV) causes cervical cancer, which is the second most frequently occurring cancer in women, but multiple sexual interactions with multiple people are one of the reasons that make young adults start diagnosed at an early age. Over 60% in 5 years is not a small number to highlight risk factors for human papillomavirus (HPV) infection, which include the number of lifetime sex partners, which is a very risky factor. Naturally, a history of human papillomavirus (HPV) infection includes viral tenacity, immune response, development of lesions, and development to cancer. Over 40 HPV types infect the human anogenital tract including the genital and anal area and perianal and genital region.15 HPV types have been classified as high risk for the development of cervical cancer, 3 HPV types are classified as expected to be high risk, and 12 HPV types have been classified as low risk.[6,7] Human papillomavirus (HPV) is probably the most common STD, with 75% of sexually active adults in the United States demonstrating clinical or serological evidence of

infection by genital Human papillomavirus (HPV) type. Young age < 25 years is strongly associated with a higher prevalence of human papillomavirus(HPV).[8] Human papillomavirus (HPV) DNA was detected at initial examination in 56% of human papillomavirus–seropositive and 31% of human papillomavirus–seronegative individuals. Human papillomavirus (HPV) DNA is 2-3 times as frequent in cervicovaginal–lavage specimens. Persistent infection with a certain type of human papillomavirus is necessary for the development of cervical cancer. Women enrolled in this study for periodic human papillomavirus (HPV) DNA testing.[9] Most head and neck cancers are derived from the mucosal epithelium in the oral cavity, pharynx, and larynx and are known collectively as head and neck squamous cell carcinoma (HNSCC). The seven most common diseases in the world are head and neck cancer. Tobacco use, oncogenic viruses, and alcohol abuse. Human papillomavirus and Epstein-Barr virus are the predominant risk factors. Head and Neck are challenging to treat, sequencing a multidisciplinary approach with surgery, radiotherapy, and systemic therapy. It accounts for less than 5% of all cases and less than 3 % of all cases of deaths. Alcohol and smoking are one of the most common sites of risk factors in the younger population, which is also associated with human papillomavirus (HPV).[10,12] A major, statistically significant improvement in survival was observed, with the overall 5-year relative survival rate going from 55.4% in 1992 -1996 to 65.9% in 2002-2006 Improvement in cancers of the oral cavity, tongue, tonsils, and nasopharynx, with the greatest improvement observed in head and neck squamous cell carcinoma (HNSCC.).[13]

Human papillomavirus mechanism

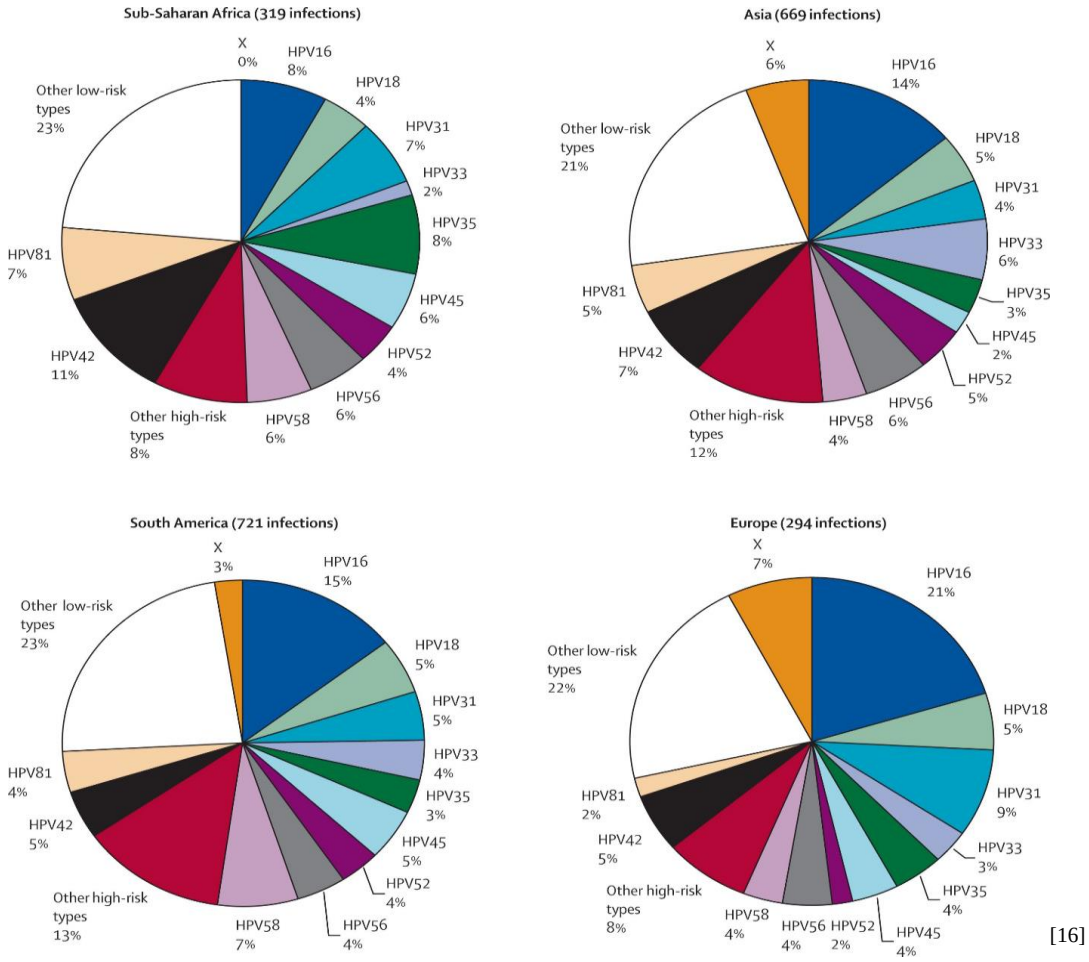
Papillomaviruses are small nonenveloped viruses with a 55-nm-diameter icosahedral capsid, which refers to the geometrical shape of a capsule composed of protein subunits and has the shape of an icosahedron—a 3D figure with 20 identical triangular faces, 12 vertices, and 30 edges. They are widely distributed throughout the animal kingdom, specifically infecting squamous epithelia infectious etiology of warts was suspected and eventually proven in the 19th century. Genital warts and cervical cancer are common venereal diseases, such as syphilis and gonorrhoea. The concept that some warts have an inherent affinity for malignant progression was established from studies by Shope, Pous, and others who studied experimental transmission on rabbits for naturally occurring cottontail. These investigators discovered that lesions formed by inoculation with cottontail rabbit wart extract, particularly in malignant progression. Carefully transmission studies demonstrated that such extract caused the emergence of warts only in rabbits and not in other animals, thus species

specificity of papillomavirus. Approximately 200 different HPVs have now been characterized, and new types of viruses can be classified into mucosal and cutaneous HPVs. Individual viruses are shown as high risk or low risk according to their tendency for malignant progression. Among the cutaneous HPV types, HPV-5 and HPV-8 may be classified as high risk, as they are associated with the development of Epidermodysplasia verruciform (EV), an exceedingly rare skin condition that provides the earliest indications that HPVs may contribute to tumour formations. Epidermodysplasia verruciform (EV) patients present with flat wart-like cutaneous lesions in early childhood and frequently develop skin cancers, particularly in sun-exposed epithelial sites.HPV-5- and HPV-8-related HPVs have been detected in a large percentage of nonmelanoma skin cancers, particularly those that develop in immunosuppressed patients. There have been few molecular studies with EV-type HPVs that yield insights into the molecular pathways by which these viruses may contribute to skin oncogenesis.[14]

Human papillomavirus percentage in southern countries

The worldwide prevalence of infection of human papillomavirus (HPV) in women without any cervical abnormalities that up to 11-12%, with higher rates in sub-Saharan Africa (24%), Eastern Europe (21%) and Latin America (16%), the most prevalent types are HPV16 (3.2%) and HPV 18 (1.4%). Estimates of these incidence of human papillomavirus cancers for 2008 due to infection have been calculated globally, with an estimated 12.7 million cancers occurring in 2008; 610,000 (Population Attributable Fraction [PAF]=4.8%)could be attributable to infection. The PAF varies substantially by geographic region and level of development, increasing to 6.9% in less developed regions, 1.6% in North America, and 1.2% in Australia/NEW Zealand. For Cervical cancer, the PAF is estimated to be 100%, accounting for 530,000(86.9%) of the HPV attributable cases, with the other five cancer types that are accounted for the residual of 80,000 cancers cases. Cervical cancer is the third most common female malignancy. It shows a strong association with the level of development rate, being at least four-fold countries defined within the low ranking of the human development index (HDI) compared with those in the very high ranking countries. A lack of information from low HDI countries, where screening is likely to have been successfully implemented. Estimates the projected incidence rates appear to be consistently declining by approximately 2 % per annum, and estimates of the projected incidence of cervical cancer in 2030, based entirely on demographic factors that indicate 2% increase in prevalence across the globe of cervical cancer, i.e., reduction in cervical cancer decreasing globally with existing trends..

Due to the relatively small number involved, it is difficult to detect temporal trends for the other cancers associated with HPV infection. Reliable surveillance figures are difficult to obtain, but data from developed countries indicate an annual incidence of 0.1 to 0.2%, with a peak occurring at teenage and young adult ages.[15]



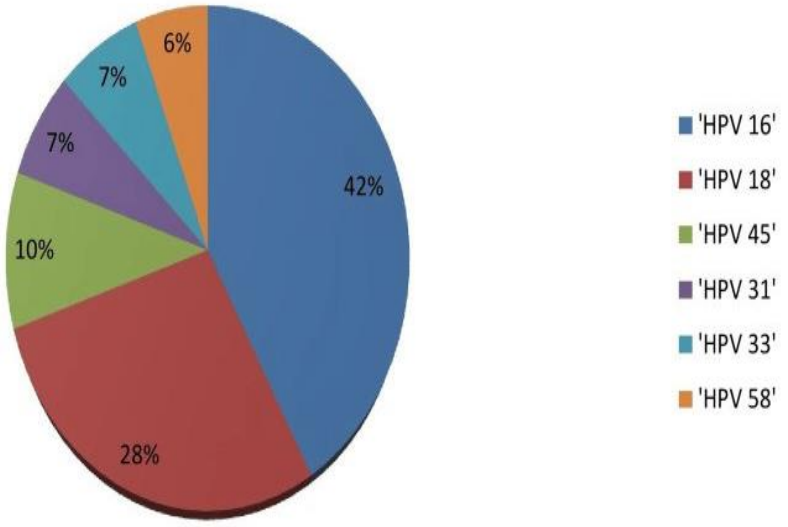
[16]

Human papillomavirus risk for Women and Why?

Cervical cancer is the most common cancer and a leading cause of death among women in developing countries. The disease is caused due to persistent infection have high-risk human papillomavirus (HPV), most commonly type in India, over 98% of cervical cancer cases in HPV infection and HPV 16 is the type exclusively 80-90%. Unlike the West, HPV infection is most common in sexually active women aged 26-35 years of sexually active, and invasive cancer also arises much later, with a peak at about 45-55 years of age. Cancer of the cervical canal passage within the cervix is the second most common cancer worldwide, with an estimate of 493,000 new cases and 274,000 deaths due to cervical cancer in 2002, the majority of over 80% of cases occurring in developing countries. In India, cervical cancer is a leading cancer with an annual incidence of about 130,000 cases and 70-75,000 deaths.[17] The

target population for this analysis was all adolescent girls, although risk factors for HPV infection are identifiable, to evaluate a universal vaccination program for several reasons. Incidence of HPV infection was based on Mayer's mathematical model of HPV infection annual incidence began at age 15 (10%), peaked at age 19 (18%), and dropped off quickly after age 29(1%). No prevalent HPV infections existed in initial cohort of 12-year-old girls, but varied assumptions in sensitivity analyses.[18] Although the risk of human papillomavirus (HPV)- associated cancers of the anus, cervix, oropharynx, penis, vagina, and vulva is increased among persons with AIDS, the etiologic role of immune suppression therapy and incidence trends for these cancers over time, particularly after introduction of highly active antiretroviral therapy in 1996.[19]

Distribution of high -risk hpv geno type in india



[20]

Head and Neck

Sex and country-specific rates of HNC were calculated for 1998-2002 and 1983-1987 using population-based data assembled by the Cancer Incidence in Five Continents (CI5) data system for 83 registries representing 35 countries. Head and Neck cancer (HNC) are categorized into three groups: oral cavity includes tongue and mouth, in which oropharynx includes tonsils and oropharynx, and other groups of HNC include larynx and poor cases that are specified tumours of the lip/ oral/ cavity/pharynx. Age-standardized rates as per used 100,000 persons were calculated using the 1960 world standard population. Changes in rates between 1998-2002 and 1993-1987 were assessed.[21] Human papillomavirus may play an important role in the etiology of Head and Neck squamous cell carcinoma (HNSCC), particularly for tumours of the oropharynx. Proteins that are found in the oncogenic causes a

high-risk type of HPV, such as HPV-16, can bind to the P53 protein and accelerate its degradation, ability to inhibit the growth of, induce apoptosis, or cause substantial genetic damage to head and neck cancer cells.[22]

Etiology

Through a large number of health surveillance research studies, a strong link has been found between the use of tobacco and increase risk for Head and Neck squamous cell carcinoma (HNSCC). Mutagenic exposure to tobacco, alcohol, or the areca nut is the major cause of environmental carcinogenesis, leading to Head and Neck squamous cell cancer (HNSCC). Exposure to carcinogens, macro-level societal conditions that result in exposure to second-hand smoke, pollution, and also contribute to increasing the risk factor. Both proximal and distal risk factors for environmental Head and Neck squamous cell carcinoma are associated with a major challenge in developing countries. In the United States, there has been a decrease in overall tobacco use, which has led to a simultaneous reduction in overall tobacco use. The risk for the development of oral cancer is 3 to 9 times greater in those who smoke or drink, and as much as 100 times greater in those who neither smoke nor drink. Mutations of P53 have been found more frequently in Head and Neck squamous cell carcinoma of smokers and drinkers as compared to those of other patients. Inactivation of the P53 tumour suppressor gene is important in tobacco-induced Head and Neck squamous cell carcinoma tumorigenesis. A total of 63.8 % of patients with oropharyngeal cancer (206 of 323) have human papillomavirus–positive tumours; these patients had better 3-year rates of overall survival, 82.4% vs 57.1% among patients with human papillomavirus–negative tumours $P<0.001$ by the log rank test after adjustment for age, race, tumours, and nodal stage, Tabacco exposure, and treatment assignment, had reduce 58% of risk to death. Using looping partition analysis**,** classified patients having a low intermediate or high risk of death on the basis of four factors:

- Human papillomavirus status
- Pack–years of tobacco
- Smoking tumour
- Nodal stage.[23,25]

Head and Neck current techniques

Benefits of IMRT

Intensity modulated radiotherapy (IMRT) is an advanced approach to 3-D treatment planning and conformal therapy. It optimises the delivery of irradiation to irregularly–shaped volumes and has the ability to produce concavities in radiation treatment volumes. It allows for greater sparing of normal structures such as salivary glands, upper aero-digestive tract mucosa, optic nerve, cochlea, pharyngeal constrictor muscle, brain stem, and spinal cord. Patients mostly undergoing radiation therapy technique for head and neck cancer (HNC) mostly experience significant early and long-term side effects. Late side effects include: permanent loss of saliva, osteoradionecrosis, radiation recall myositis, pharyngoesophageal stenosis, dental caries, oral cavity necrosis, fibrosis, impaired wound healing, skin changes, and skin cancer, but in secondary cancer, eye, ear, neurological, and neck structures are shown as late symptoms. Patients who undergo radiotherapy for nasopharyngeal carcinoma tend to suffer from chronic sinusitis.[26,27]

Image–guided radiotherapy (IGRT)

IMRT, simplest form, can be used to minimise the geographical miss resulting from changes in the patient anatomy. Studies have demonstrated the sociometric changes resulting from volume alteration in tumours and organs at risk. Adaptive radiotherapy using regular.

Volumetric intensity modulated therapy (VMAT)

Volumetric intensity modulated arc therapy (VMAT) is a newer technique of delivering IMRT.VMAT delivers IMRT-like distributions in a single rotation of the gantry, varying the gantry speed and dose rate during delivery in contrast to standard IMRT, which uses fixed gantry beams. This technique has been implemented in Eclipse treatment planning software (Varian Medical Therapy System, Palo Alto, CA) under the name Rapid Arc (RA).

Particle therapy

Charged particles like protons deposit little energy until they reach the end of their range (depending on their energy), at which point most of the energy is deposited in a small area, known as the Bragg peak. These advantages in terms of normal tissue sparing, better dose homogeneity, and reduced dose bath effect (low radiation dose to normal tissue). Intensity modulated proton therapy (IMPT) allows modulation of the fluence and the position of the Bragg peak.

CONCLUSION

The transforming activity of high-risk human papillomavirus represents the consequence of the viral replication strategy replicates viral genomes, normally growth–arrested differentiated epithelial cells, and establishes in individual cells rapidly turned over and shed. Low-risk human papillomavirus-specific biological activity of E6 and E7 may reflect and may have evolved a life cycle optimized to rapidly produce progeny virus readily from large productive lesions to maximize transmission of virus to a new host. A cost–effective human papillomavirus vaccine is needed for developing countries to address various issues. It is most important to make it easy to produce and distribute, human papillomavirus 16 is only oncogenic, 80% prevalent in India, and should be a major focus for the vaccine that would be highly beneficial. Risk of human papillomavirus-associated cancer is elevated among youngsters and increases with the increase in immunosuppression. Human papillomavirus is most common in many regions, majority of sexually active induvial variations in prevalence by age and a peak in HPV prevalence among young women. Head and neck techniques like intensity modulated radiotherapy (IMRT), image–guided radiotherapy (IGRT), volumetric intensity modulated therapy (VMAT), and particle therapy are some advanced surgical techniques that target therapies and radiations, have significantly improved outcomes in head and neck skin cancer. Early detection and some surgical treatment techniques play a crucial role in offering survival rates and functional preservation.

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