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內文：

1. Introduction

head and neck squamous cell carcinoma→ (HNSCC)

high-risk HPV →(hrHPV)

1.Human papillomaviruses (HPVs) are small nonenveloped DNA viruses that infect squamous epithelial cells

2. more than 100 different genotypes, approximately 15 are considered oncogenic

3. low-risk HPV subtypes→benign neoplasms,ex ： papillomas ； high-risk subtypes→malignant neoplasms

4.HPV-positive HNSCC is a biologically distinct entity different from tobacco- and alcohol-associated carcinom→oral and oropharyngeal；better patient survival because increased sensitivity to radiation therapy

5. in situ hybridization(ISH) technique→allows for the visualization of HPV localization within the tumor cells.

2. Materials and methods

1.Time ：January 2000 and December 2004；January 2009 and October 2010

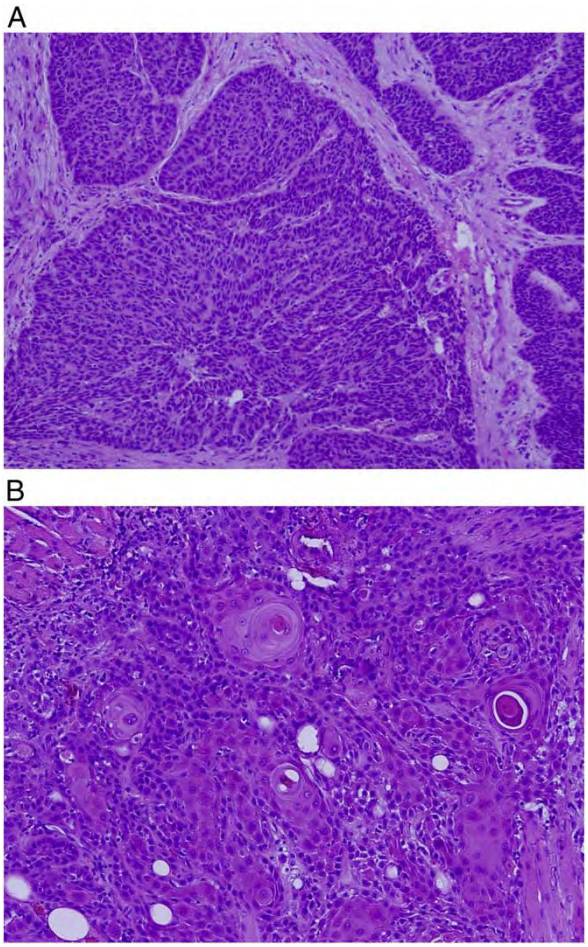
2.excluded 1. tissue specimens were too small 2. no tumor tissue was identified

3.The probe used is capable of hybridizing with hrHPV genotypes 16, 18, 33, 35, 45, 51, 52, 56, and 66.

4.Positive→dark blue punctate (dotlike) or diffuse nuclear signals in confluent groups of tumor cells

5.Locations：oral cavity, larynx, oropharynx(soft palate, the tonsil, and the base of tongue), hypopharynx, and nasopharynx

6.histologic types ： nonkeratinizing squamous cell carcinoma (NKSCC) and keratinizing squamous cell carcinoma (KSCC)



1. Nonkeratinizing squamous cell carcinoma composed of invasive sheets, nests, or trabeculae of tumor cells with squamous differentiation but no evidence of distinct keratinization (A).
2. Keratinizing squamous cell carcinoma composed of recognizable squamous tumor cells with pronounced keratinization (B) (original magnification ×200).

3.Results

Table 1
Head and neck squamous cell carcinoma study population (2000-2004) grouped by hrHPV status

Total	HPV, 142; n (%)	HPV negative, 124; n (%)	HPV positive, 18; n (%)
Sex			
Male	99 (70)	86 (69)	13 (72)
Female	43 (30)	38 (31)	5 (28)
Race			
Black	55 (39)	49 (40)	6 (33)
White	75 (53)	66 (53)	9 (50)
Unknown	12	9	3
Smoking and drinking			
Smoking	98 (70)	86 (69)	12 (67)
Nonsmoking	13 (9)	11 (9)	2 (11)
Unknown	31 (21)	27 (22)	4 (22)
Drinking	69 (48)	62 (50)	7 (39)
Nondrinking	37 (26)	30 (24)	7 (39)
Unknown	36 (26)	32 (26)	4 (22)
Anatomical site			
Oropharynx	24 (17)	15 (12)	9 (50)
Tonsils	7 (5)	3 (2)	4 (22)
Nontonsil	17 (12)	12 (10)	5 (28)
Nonoropharynx	118 (83)	109 (88)	9 (50)
Oral cavity	69 (49)	62 (50)	7 (39)
Larynx	44 (31)	42 (34)	2 (11)
Hypopharynx	4 (3)	4 (3)	0
Nasopharynx	1 (1)	1 (1)	0

Table 2
Head and neck squamous cell carcinoma study population (2009-2010) grouped by hrHPV status

	Total, N = 35; n (%)	HPV negative, n = 21; n (%)	HPV positive, n = 14; n (%)
Sex			
Male	27 (77)	14 (67)	13 (93)
Female	8 (23)	7 (33)	1 (7)
Race			
Black	9 (26)	9 (43)	0
White	24 (69)	11 (52)	13 (93)
Asian	1 (3)	1 (5)	0
Unknown	1 (3)	0	1 (7)
Smoking and drinking			
Smoking	27 (74)	19 (92)	8 (55)
Nonsmoking	7 (26)	2 (8)	5 (45)
Unknown	1 (3)		1 (7)
Drinking	22 (63)	16 (76)	6 (43)
Nondrinking	10 (29)	5 (24)	5 (36)
Unknown	3 (9)		3 (21)
Anatomical site			
Oropharynx	23 (66)	10 (48)	13 (93)
Tonsils	14 (40)	5 (24)	9 (64)
Nontonsil	9 (26)	5 (24)	4 (29)
Nonoropharynx	12 (34)	11 (52)	1 (7)
Oral cavity	8 (23)	8 (38)	0
Larynx	3 (6)	2 (10)	1 (7)
Nasopharynx	1 (3)	1 (5)	

Table 3
Clinical characteristics of total HNSCC study population and HPV status

	Total, N = 177; n (%)	HPV negative, n = 145; n (%)	HPV positive, n = 32; n (%)	*P* (Fisher exact test)
Mean age (y)		57		58
Sex				
Male	126 (71)	100 (69)	26 (81)	.1994
Female	51 (29)	45 (31)	6 (19)	
Race				
African	64 (36)	58 (40)	6 (19)	.036
White	99 (56)	77 (53)	22 (69)	
Asian	1 (1)	1 (1)		
Unknown	13 (7)	9 (7)	4 (13)	
Smoking and drinking				
Smoking	125 (71)	105 (72)	20 (62)	.0607
Nonsmoking	20 (11)	13 (9)	7 (22)	
Unknown	32 (18)	27 (19)	5 (16)	
Drinking	91 (51)	78 (53)	13 (41)	.1103
Nondrinking	47 (27)	35 (24)	12 (38)	
Unknown	39 (23)	32 (23)	7 (22)	

Table 4
Histologic classification of all HNSCC and associated characteristics

	Total	KSCC, 121; n (%)	NKSCC, 56; n (%)	*P* (Fisher exact test)
Age		57.5	56.5	
Sex				
Male	126	82 (68)	44 (79)	.15
Female	51	39 (32)	12 (21)	
P				
Smoker				
Yes	125	84 (69)	41 (73)	1.00
No	20	14 (12)	6 (11)	
Unknown	32	23 (19)	9 (16)	
Drinker				
Yes	91	60 (50)	31 (55)	.7029
No	47	33 (27)	14 (25)	
Unknown	39	28 (23)	11 (20)	
HR-HPV-ISH (%)				
Positive	31	12 (10)	20 (36)	.0001
Negative	145	109 (90)	36 (64)	
Anatomical site				
Oropharynx	47	20 (17)	27 (48)	
Tonsils	21	9 (7)	12 (21)	.0001 (oropharynx vs nonoropharynx)
Nontonsil	26	11 (9)	15 (27)	
Nonoropharynx	129	101 (83)	29 (52)	
Oral cavity	77	64 (53)	13 (23)	
Larynx	47	34 (28)	13 (23)	
Nasopharynx	2	0	2 (4)	
Hypopharynx	4	3 (2)	1 (2)	
Racial				
African	64	43 (36)	21 (38)	1.000
White	99	67 (55)	32 (57)	
Asian	1	1 (1)		
Unknown	13	10 (8)	3 (5)	

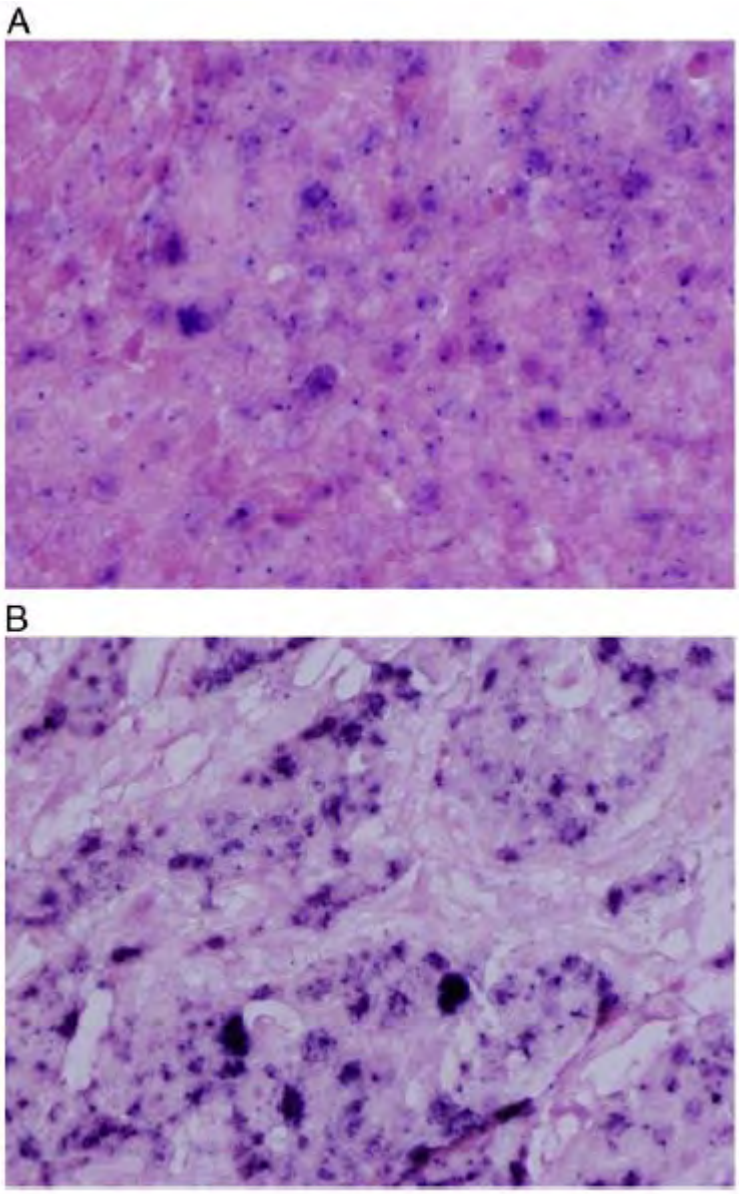


Fig. 2. Dark blue punctate (dotlike, A) or diffuse nuclear staining patterns(single or multiple intranuclear spots of variable size, B) of hrHPV-positive tumor cells (original magnification ×400).

1. Discussion

1. 85% of humans will have HPV infection of any subtype during their lifetime

2.in situ hybridization(ISH) technique
→routine use、localization of HPV DNA in a specimen、high specificity
polymerase chain reaction (PCR)
→sensitive、expensive

3. demographics→tobacco and alcohol widespread in our patient 、no age difference

4. increased prevalence of HPVassociated head and neck cancers：
from13% in the 2000-to-2004 series to 40% in the 2009-to-2010 series.
→2000-to-2004： low percentage of tumors from the oropharyngeal sites and high frequency of smoking and drinking history in our patients;
→2009-to-2010： increasing community awareness and screening coupled with the

introduction of routine testing for hrHPV DNA
5. oropharynx than other head and neck sites→The low rate (8%) of HPV-positive nonoropharyngeal SCC due to smoking and drinking habits
6. African Americans have a higher incidence of HNSCC with high mortality rate：heavy alcohol and tobacco use
7. HPV-related SCC of the oropharynx nonkeratinizing：better patient survival

題號	題目 下列對HPV描述何爲非
1	(A) 菜花爲 HPV〉所引起大部份是經性行爲傳染, 長出的位置大部分在外陰部及會陰男性的龜頭、包皮、陰莖， 女性的大小陰唇是好發的地方 (B) 位於 口腔粘膜的菜花可能通過口交而受到傳染 (C) 病毒可存於健康的人體 因多無症狀 而不被察覺多數的輕度 HPV 感染者都可自行痊癒 (D) 有些 HPV 與口腔與喉部的癌症關係不大
答 案 (D)	出處：
題號	題目 對於 HPV 病毒，何為非
2	(A) Verruca vulgaris 和HPV 2、4、6、40 感染有關，小孩常見，多在手或 lip 上，papillary 外型 (B) HPV 會引發 Verruciform xanthoma (C) 和 scc 高度相關的有 16 和 18 (D) HPV 感染的情況下,組織切片下可見 Koilocytes
答 案 (B)	出處：不會引發