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Original Article

Correlation of human papilloma virus with oral squamous cell carcinoma in Chinese population

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Abstract: Previous studies indicated that oral squamous cell carcinomas (OSCC) might be related to human papilloma virus (HPV) infection. However, the relationship between OSCC in a Chinese population and oral HPV infection is still unclear. In this study, we evaluate the relationship of OSCC with HPV infection in a Chinese population via a meta-analysis. The reports on HPV and OSCC in a Chinese population published between January, 1994, and October, 2015 were retrieved via CNKI/WANFANG/pubmed databases. According to the inclusion criteria, we selected 26 eligible case-control studies. After testing the heterogeneity of the studies by the Cochran Q test, the meta-analyses for HPV and HPV16 were performed using the random effects model. Quantitative meta-analyses showed that, compared with normal oral mucosa the combined odds ratio of OSCC with HPV infection were 1.98 (95% CI: 1.34-2.92). The test for overall effect showed that the *P* value was less than 0.05 (Z=3.46). Forest plot analyses were seen in Figures 2 and 3. Publication bias and bias risk analysis using RevMan 5.3 software were measured indicators of the graphics of the basic symmetry. High incidences of HPV infection were found in the samples of Chinese OSCC. For the Chinese population, HPV infection elevates the risk of OSCC tumorigenesis.

Keywords: Human papilloma virus, oral squamous cell carcinoma, Chinese

Introduction

HPV infection is a cause of nearly all cases of cervical cancer. In 1983, OSCC was firstly reported to be associated with HPV infection [28]. Afterwards, many studies showed that a different degree of relationship might exist between OSCC and HPV infection. It is possible that the risk difference of OSCC with HPV infection varies from different regions and different populations. Over 90% of all cervical cancers can be attributed to certain HPV types-HPV16 accounting for the largest proportion (roughly 50%) followed by HPV18 (12%), HPV 45 (8%), and HPV 31 (5%) [1]. Worldwide in 2002, an estimated 561,200 new cancer cases (5.2% of all new cancers) were attributable to HPV, suggesting that HPV is one of the most important infectious causes of cancer [2]. In recent years, some studies by Chinese researchers have also focused on the relationship between oral squamous cell carcinoma (OSCC) and HPV oral infection.

However, the differences of the odds rates were reported in different literatures. Therefore, it is necessary to implement a meta-analysis which aims to comprehensively evaluate the relationship between OSCC and HPV oral infection in a Chinese population.

Methods

Search strategy

The keywords HPV, human papillomavirus, oral, oral cancer, head and neck cancer, tongue cancer, squamous cell carcinoma, oral carcinoma, buccal cancer, oral lesions, and Chinese population. The retrieved databases included China National Knowledge Infrastructure (CNKI)/Wanfang Database/OVID/MEDLINE. Finally, a total of 401 citations published between Jun, 1994 and Oct, 2015 were identified.

Inclusion and exclusion criteria

The literatures included in the present study meets the following criteria: case-control stud-

Table 1. Characteristics of studies investigating human papillomavirus (HPV) infection in oral squamous cell carcinoma (OSCC) and control samples

First author	Year	Gender		HPV(-)	HPV(+)	Mean age	Country	Method
		F	M					
Huang CG [6]	2014	16	296	260	52		China	PCR
Chen YW [7]	2012	21	144	109	56	52	China	Immunostaining
Huang SF [8]	2012	7	96	72	31	49	China	PCR
Simonato LE [9]	2008	2	27	5	24	23	Brazil	PCR
Oliveira LR [10]	2007	14	73	17	70	54	Brazil	PCR
Duray A [11]	2012	32	130	44	65	57	Belgium	PCR Immunohistchemistry
Zhao D [12]	2009	17	35	21	21	-	China	PCR
Schwartz SR [13]	2001	90	163	40	214	54.2	America	PCR
Lee LA [14]	2012	7	156	135	71	51	China	PCR
Metgud R [15]	2012	72	156	162	66	-	America	PCR
Elango KJ [16]	2011	19	41	31	29	55	India	PCR
Chen SF [17]	2012	13	52	41	24	53	China	In situ hybridization
Kruger M [18]	2014	32	56	83	5	-	Germany	PCR
Meyer MF [19]	2014		-	68	25	57	Germany	PCR
Woods KV [20]	1993	7	11	4	14	61	America	PCR
Kozomara R [21]	2005	-	-	18	32	32	Yugoslavia	PCR
Gonzalez-Ramirez I [22]	2013	46	34	76	4	63	Mexico	PCR
Gan LL [23]	2014	57	143	145	55	81	China	PCR
Goot-Heah K [24]	2012	21	9	29	1	30	Malaysia	PCR
Harris SL [25]	2011	15	10	14	11	30	America	In situ hybridization (ISH)
Laco J [26]	2012	-	-	22	2	63	Hradec Kralove	PCR
Campisi G [27]	2006	35	28	39	24	68.89	Italy	PCR
Lee LA [28]	2013	19	391	323	87	52	China	In situ hydridisation
Melchers LJ [29]	2015	70	106	175	1	63	Netherlands	In situ hydridisation

ies; Chinese population; a diagnostic method was addressed and reliable. The literatures excluded in this study were mainly due to the following reasons: lacks of data needed; reviews. Of 401 publications identified through an initial search of databases and conference abstracts, 375 were excluded. A total of 26 literatures met the eligibility criteria were included in this present study.

Data extraction

The data related to this study were extracted by two independent reviewers. Any discrepancies were resolved by consensus or in consultation with a third reviewer. The data related to this study were shown in **Table 1**.

Data analysis

The dichotomous data of HPV positive results in OSCC group and normal control group was summarized. OR and 95% confidence interval [CI] of OR were calculated for assessing the association between HPV infection and OSCC risk. The analysis of the heterogeneity of between-study was performed using the Chi-square-based Q test [3]. A *P* value less than 0.05 was considered significant for the heterogeneity. If no heterogeneity, a fixed-effect model was applied using the Mantel-Haenszel method [4]. Otherwise, the random-effect model with the DerSimonian-Laird method [4] was used. The potential publication bias was assessed graphically by funnel plots [5]. The statistical analyses were performed using RevMan 5.3.

Results

The mainly character of study included is showed in **Table 1**. Tests for the heterogeneity showed that, the Chi-square values were 655.89 ($P<0.05$). Therefore, a random-effect

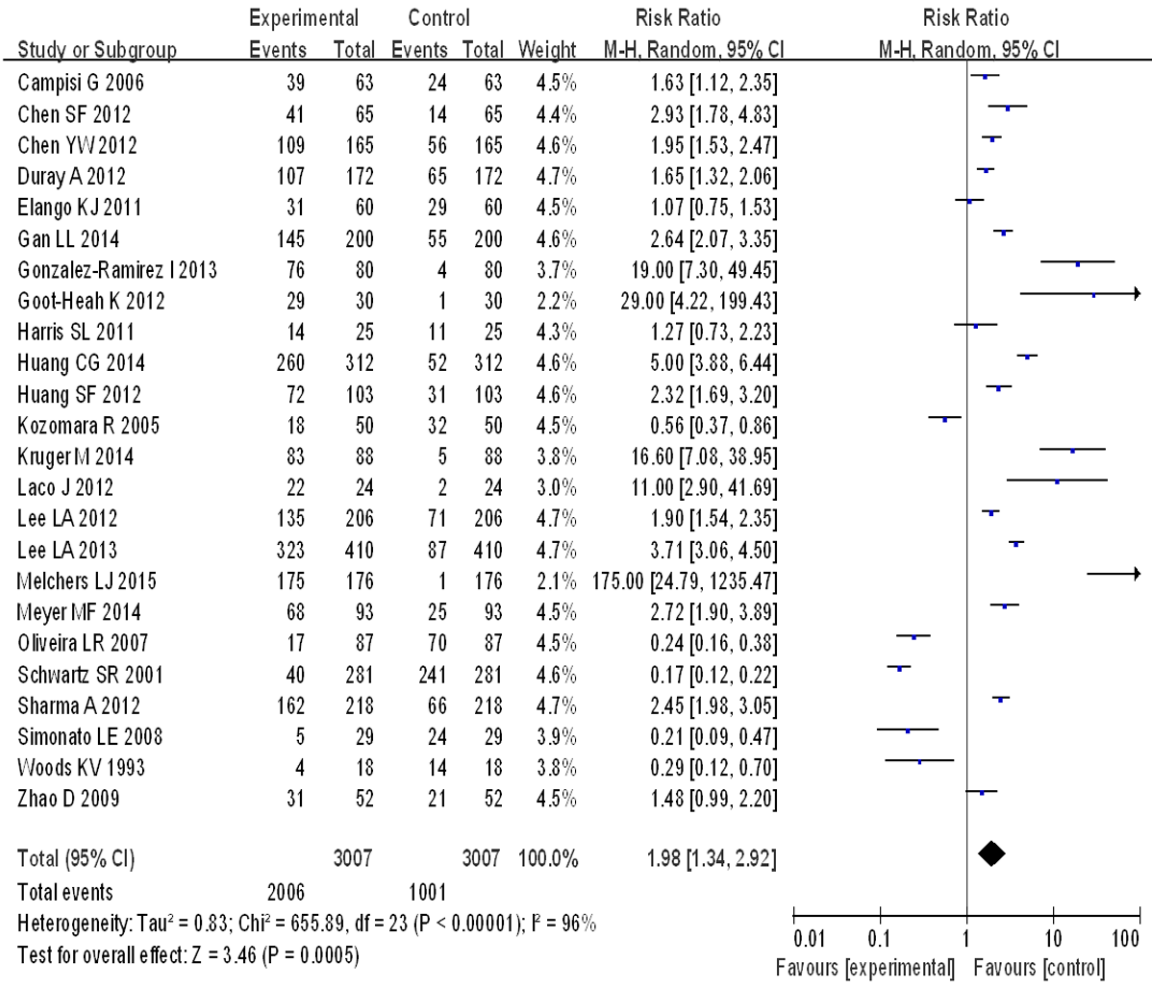

Figure 1. Forest plots of the included studies of oral squamous cell carcinoma risk in HPV infection.

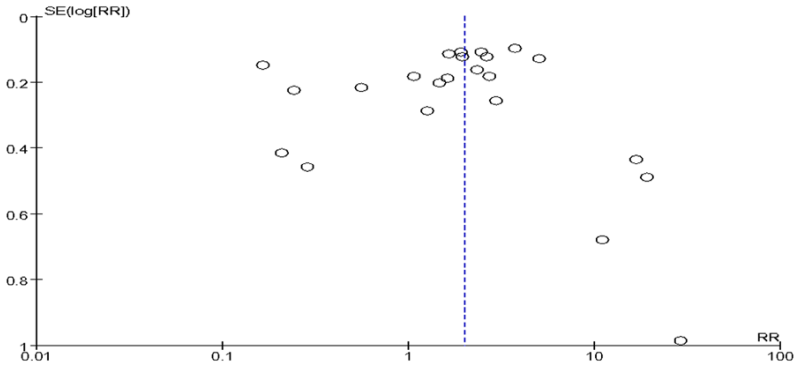

Figure 2. Funnel plot of the included studies of oral squamous cell carcinoma risk in HPV infection.

model was applied. Quantitative meta-analyses showed that, compared with normal oral mucosa the combined odds ratio of OSCC with HPV infection were 1.98 (95% CI: 1.34-2.92) (**Figure 1**). The test for overall effect showed that the *P* value was less than 0.05 (Z=3.46). Forest plot analyses were seen in **Figure 2**. Publication bias and bias risk analysis using RevMan 5.3 software were measured indicators of the graphics of the basic symmetry (**Figures 3**, **4**).

Discussion

Quantitative meta-analyses showed that, compared with normal oral mucosa the combined odds ratio of OSCC with HPV infection were 1.98 (95% CI: 1.34-2.92). While another previous meta-analysis of the included literatures published in English-language journal between 1980 and 1998 revealed that [30], the likelihood of

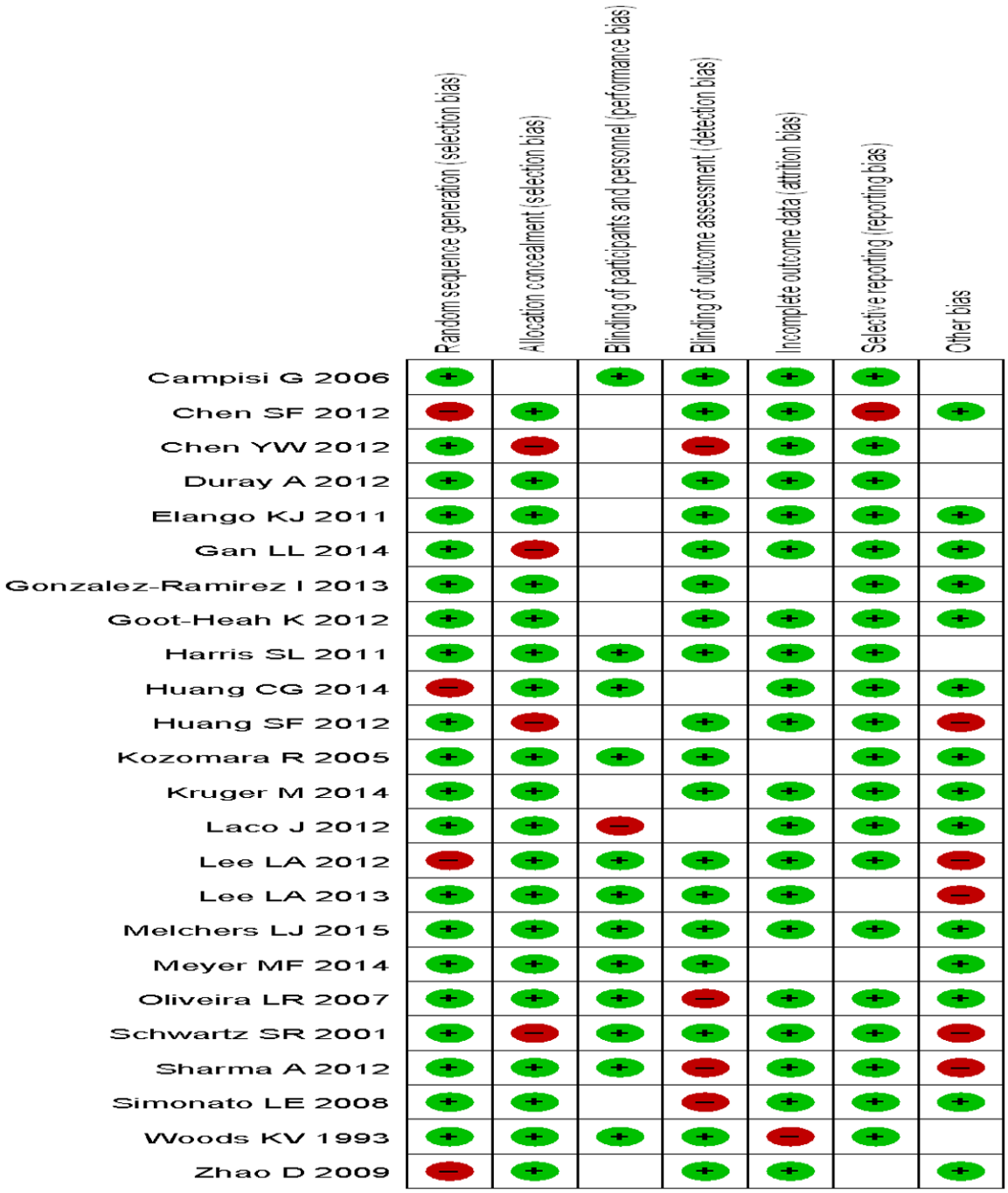

Figure 3. Risk of bias summary.

detecting HPV in normal oral mucosa (10.0%; 95% [CI], 6.1%-14.6%) was significantly less than that of OSCC (46.5%; 95% CI: 37.6%-55.5%), and the pooled odds ratio for the subset of studies directly comparing the prevalence of HPV in normal mucosa and OSCC was 5.4.

The previous reports showed that the patients with HPV-positive oropharyngeal cancers had a lower risk of dying or recurrence than do those with HPV-negative cancers [31-33]. The majority of studies showed than HPV-associated OSCC were associated with a better prognosis than HPV-negative tumors in the majority of

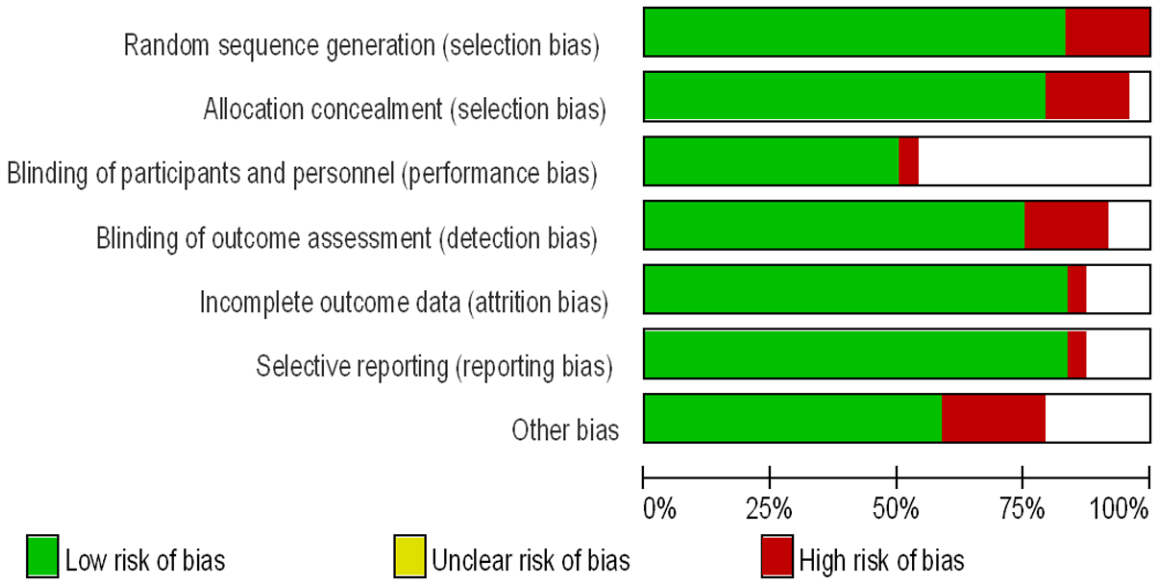

Figure 4. Risk of bias graph.

studies [34, 35]. Some researcher found that HPV-positive conferred a 60% to 80% reduction in risk of death from cancer compared with HPV-negative tumors [36]. Thus, HPV screening to the patients with OSCC is good for assessing the prognosis of OSCC. Prophylactic HPV-vaccination may reduce the burden of HPV-related OSCC in China.

In present study, the funnel plots of included studies showed that, the graphics is basically symmetric and all points is concentrated in the central funnel, indicating that no publication bias was found in this study. Additionally, the present study also has some shortcoming. Most of the literatures included the present study didn't control confounding factors, because gender, age, and lifestyle have a big influence on the relationship between OSCC with HPV infection. Moreover, tumor location, clinical stage and degree of differentiation also have some degree of effect on the association mentioned above. Considering that HPV infection plays an important role in tumorigenesis of OSCC, more scientific studies should be included for meta-analysis in future research.

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Disclosure of conflict of interest

None.

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