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Alcohol consumption and persistent infection of high-risk human papillomavirus

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SUMMARY

Alcohol consumption is a possible co-factor of high-risk human papillomavirus (HR-HPV) persistence, a major step in cervical carcinogenesis, but the association between alcohol and continuous HPV infection remains unclear. This prospective study identified the association between alcohol consumption and HR-HPV persistence. Overall, 9230 women who underwent screening during 2002–2011 at the National Cancer Center, Korea were analysed in multivariate logistic regression. Current drinkers [odds ratio (OR) 2·49, 95% confidence interval (CI) 1·32–4·71] and drinkers for ⩾5 years (OR 2·33, 95% CI 1·17–4·63) had a higher risk of 2-year HR-HPV persistence (HPV positivity for 3 consecutive years) than non-drinkers and drinkers for <5 years, respectively (*vs.* HPV negativity for 3 consecutive years). A high drinking frequency (⩾twice/week) and a high beer intake (⩾3 glasses/occasion) had higher risks of 1-year (OR 1·80, 95% CI 1·01–3·36) HPV positivity for 2 consecutive years) and 2-year HR-HPV persistence (OR 3·62, 95% CI 1·35–9·75) than non-drinkers. Of the HPV-positive subjects enrolled, drinking habit (OR 2·68, 95% CI 1·10–6·51) and high consumption of beer or soju (⩾2 glasses/occasion; OR 2·90, 95% CI 1·06–7·98) increased the risk of 2-year consecutive or alternate HR-HPV positivity (*vs.* consecutive HPV negativity). These findings suggest that alcohol consumption might increase the risk of cervical HR-HPV persistence in Korean women.

Key words: Alcohol, cervical carcinogenesis, co-factors, human papillomavirus, persistence.

INTRODUCTION

Human papillomavirus (HPV) infection has been established as the primary cause in the development of cervical intraepithelial neoplasia (CIN) and cervical cancer [1]. However, HPV infections are usually transient and mostly regress to a virus-free status or low-grade lesions [2]. By contrast, persistent infection with carcinogenic HPV genotypes causes CIN lesions and cervical cancer development [2, 3]. HPV persistence has been reportedly associated with viral variants such as viral genotypes, multiple infections, and viral loads [4] as well as host genetic variability, especially in genes that control the immune response [5]. Several host epidemic characteristics including older age [2, 6], multiple sexual partners [2, 7], smoking [7], individual immune responsiveness [8], and oral

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contraceptive use [9] have also been reportedly associated with HPV persistence, but the results related to these epidemiological factors are highly controversial.

Alcohol is a potential risk factor of oral, oesophageal, colorectal, and liver cancers [10] and has been reported to increase the risk of breast, endometrial, and ovarian cancers by enhancing oestrogen levels and metabolism [11]. However, epidemiological evidence for cervical cancer is lacking and controversial [12]. Alcohol is known to be a potential risk factor of HPV infection (acquisition), but there are few studies on the association of alcohol consumption and HPV persistence [2, 13]. Furthermore, no studies have reported on specific alcohol consumption behaviours such as frequency, duration, and specific types of alcoholic beverages consumed, relative to HPV persistence.

The aim of our prospective study was to investigate the alcohol consumption characteristics (drinking status, frequency, duration of drinking, and the amount of alcoholic beverages consumed) in association with a high risk (HR)-HPV persistence according to the subjects' health screening data.

METHODS

Study design and population

A total of 10 444 Korean women who underwent health-screening examinations at the National Cancer Center from 2002 to 2011 and provided signed informed consent were included in this study. This health screening examinee study is part of the Korean Prospective Study for the Transition of Human Papillomavirus into Cervical Carcinoma (KOVIC). KOVIC is the prospective study established to identify host and environmental co-factors in the persistent HPV infection and its transformation into cervical carcinoma in Korean women. KOVIC is composed to two studies, a health examinee-based prospective study and a patient-based prospective study. There is an ongoing follow-up investigation. The study protocol was approved by the Institutional Review Boards and Ethics Committee of the National Cancer Center in Korea (NCCNCS-11-433). After excluding 558 women who did not participate in HR-HPV deoxyribonucleic acid (DNA) testing and 656 women who did not complete the questionnaire about detailed alcohol consumption behaviours, a total of 9230 women were available for HPV infection analysis. We collected HPV DNA data, cytology findings (Pap smear), and questionnaires about detailed alcohol consumption behaviours, sociodemographics, smoking history, parity, menopausal status, and oral contraceptive use for these 9230 women. Among them, 1284 and 543 women with a cytological result of low-grade squamous intraepithelial lesion (LSIL) or less for the study period were available for 1- and 2-year follow-up studies, respectively, after excluding six subjects. Five subjects and one subject had cytology findings of high-grade squamous intraepithelial lesion (HSIL) or worse in the 1- and 2-year follow-up, respectively.

Two definitions of HR-HPV persistence were used in this study. First, 1-year HPV persistence was defined as HR-HPV positivity in the enrolment year and the 1-year follow-up study year, and 2-year HPV persistence was defined as HR-HPV positivity in the enrolment year and both the 1- and 2-year follow-up study years. One- and 2-year HPV negatives were defined as HPV negativity in the 1-year follow-up study year and as HPV negativity in both the 1- and 2-year follow-up study years, respectively, after enrolment with HPV negativity. According to these definitions, 10·1% of the 9230 women were HPV positive (negative, 8301; positive, 929) at enrolment. In the follow-up study, 127 and 46 women were included in the 1- and 2-year HPV-persistence categories, and 949 and 373 women were included in the 1- and 2-year HPV-negative categories, respectively.

An additional analysis was performed to compare the statuses of those cleared of HR-HPV and those still infected by HR-HPV for the two follow-up years. Two-year consecutive or alternate HR-HPV persistence was defined as HPV positivity/HPV positivity, as HPV positivity/HPV negativity, or as HPV negativity/HPV positivity in both the next year and the subsequent year, respectively, after enrolment with HPV positivity. Two-year consecutive HR-HPV clearance was defined as HPV negativity in both the next year and the subsequent year after enrolment with HPV positivity. By this definition, 140 women (2-year consecutive or alternate persistence: 89, 2-year consecutive clearance: 51) were included in the second analysis.

Questionnaires related to alcohol consumption behaviours

General characteristics were analysed with the questionnaire that included age, height, weight, marital status, number of children, menopausal status, oral

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contraceptive use, education level, income level, and cigarette smoking status. A detailed questionnaire about alcohol consumption included drinking status (current, former, never), the frequency of alcohol consumption (once/month, 2–3 times/month, once/week, 2–3 times/week, 4–5 times/week, every day, twice/day), duration of drinking habit (<5 years, ⩾5 years), and usual consumption per drinking occasion of two alcoholic beverages, beer and soju at 200 cc and 50 cc, respectively (1 glass, 2 glasses, ⩾3 glasses). Soju is a distilled beverage native to Korea and its alcohol content is usually about 20% ethanol by volume.

HPV DNA detection and Pap smear

HR-HPV DNA detection was performed with the commercially available Hybrid capture II system (HC-II, Digene Co., USA). A chemiluminescent HPV DNA test was measured as relative light units (RLU) with a probe designed for 13 types of HR-HPV (HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68). The test results were read as positive at concentrations of ⩾1 pg/ml of RLU/cut-off ratio (RLU of specimen/mean RLU of two positive controls). The cytological grades for Pap smear reports were based on the Bethesda classification system [14]. Types of results in this system included normal cells, atypical squamous cells, LSIL, HSIL, squamous cell carcinoma, atypical glandular cells, and adenocarcinoma *in situ*.

Statistical analysis

The χ^2 test and *t* test were used to analyse differences in the distributions of categorical and continuous general variables, respectively. Multivariate logistic regression models were used to estimate the odds ratios (ORs) and corresponding 95% confidence intervals (CIs). A regression analysis was performed to assess the association between several characteristics related to alcohol consumption and HR-HPV infection (*vs.* HPV negativity) and between those and 1- and 2-year HR-HPV persistence groups (*vs.* 1- and 2-year HR-HPV negative groups, respectively). The model was adjusted for age, body mass index (BMI), marital status, parity, menopausal status, oral contraceptive use, education level, income level, and smoking habit as categorical variables indicated in Table 1. Another multivariate logistic regression analysis was performed to estimate the risk of 2-year consecutive or alternate HR-HPV persistence (*vs.* HR-HPV clearance) associated with the characteristics related to alcohol consumption after adjustment for age, BMI, parity and education level as categorical variables. The risk estimates were calculated using the non-drinkers or non-alcoholic characteristics as the non-exposure category. The statistical analysis and graphical design were performed with SAS v. 9·1 (SAS Institute, USA) and Stata v. 12·0 (Stata Corp., USA) software packages.

RESULTS

General characteristics of the study subjects at baseline

As shown in Table 1, about 50% of the 9230 enrolled subjects were drinkers (4578). The mean ages of the non-drinkers and drinkers were 50·1 and 45·5 years, respectively. The drinkers were younger (~5 years) and less obese than the non-drinkers. Most of the subjects were married, and slightly more of the drinkers were single. Fewer children (2·4 of non-drinkers *vs.* 2·1 of drinkers) and greater rates of oral contraceptive use were observed in the drinkers (18% of non-drinkers *vs.* 23% of drinkers). The drinkers were more educated than the non-drinkers, and more of the drinkers were also smokers (4% of non-drinkers *vs.* 15% of drinkers). The drinkers had a higher rate of HR-HPV infection than the non-drinkers (9% and 11% of non-drinkers and drinkers, respectively).

Alcohol consumption and the risk of HR-HPV infection

Current drinkers (OR 1·21, 95% CI 1·07–1·41) and those with a higher frequency of drinking (2–4 times/month: OR 1·28, 95% CI 1·04–1·56; ⩾2 times/week: OR 1·31, 95% CI 1·05–1·64; *P* for trend = 0·049) had higher risks of HR-HPV infection than the non-drinkers (Table 2). Women with a drinking habit for ⩾5 years had a higher risk of HR-HPV infection (OR 1·20, 95% CI 1·01–1·36) than those with a <5-year drinking habit. Increased consumption of the alcoholic beverages beer and soju was associated with increased risk of HR-HPV infection (*P* for trend <0·001 and <0·006 for glasses of beer or soju normally consumed; ⩾3 glasses of soju: OR 1·24, 95% CI 1·03–1·68).

Alcohol consumption and 1- and 2-year HPV persistence

Compared to non-drinkers, the current alcohol drinkers had higher risks of 1- and 2-year HR-HPV

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Table 1. *General characteristics of study subjects at baseline* (n = *9230*)

Characteristics	Non-drinkers (*N* = 4652, 50·4%)		Drinkers (*N* = 4578, 49·6%)		*P* value
	n	%	*n*	%	
Age, years mean (S.E.)	49·9 (0·14)		45·3 (0·13)		<0·001
⩽39 years	562	12·1	1196	26·1	<0·001
40–49 years	1714	36·8	2010	43·9	
50–59 years	1616	34·7	1085	23·7	
⩾60 years	760	16·3	287	6·3	
Obesity, mean (S.E.)	23·0 (0·05)		22·7 (0·05)		<0·001
BMI <18·5	200	4·3	222	4·9	<0·001
BMI 18·5 to <23	2182	47·0	2455	53·7	
BMI 23 to <25	1124	24·2	969	21·2	
BMI ⩾25	1139	24·5	929	20·3	
Married					
Yes	4405	98·0	4252	95·9	<0·001
No	89	2·0	184	4·2	
No. of children, mean (S.E.)	2·4 (0·02)		2·1 (0·02)		<0·001
0 or 1	413	10·3	583	15·6	<0·001
2	2223	55·6	2259	60·3	
⩾3	1360	34·0	903	24·1	
Menopausal					
No	990	30·5	1467	52·1	<0·001
Yes	2258	69·5	1349	47·9	
Oral contraceptive use					
Never	2680	81·3	2355	77·3	<0·001
User (former)	593	18·0	654	21·5	
User (current)	23	0·7	38	1·3	
Education level					
⩽ Middle school	955	21·7	756	17·2	<0·001
High school	1778	40·3	1898	43·3	
⩾ University	1676	38·0	1731	39·5	
Income (won)					
⩽200 million	646	16·9	549	14·3	0·015
200–399 million	1121	29·2	1117	29·2	
400–699 million	1421	37·1	1505	39·3	
⩾700 million	646	16·9	660	17·2	
Cigarette smoking					
Non-smoker	3763	95·8	3174	85·6	<0·001
Smoker (former)	75	1·9	176	4·7	
Smoker (current)	91	2·3	356	9·6	
HPV infection (baseline)					
Negative	4242	91·2	4059	88·7	<0·001
Positive	410	8·8	519	11·3	
HPV viral loads (baseline)					
<100 RLU/CO	301	73·4	392	75·5	0·462
⩾100 RLU/CO	109	26·6	127	24·5	
Cytological findings (baseline)					
Normal	4303	97·2	4251	96·6	0·280
ASCUS	85	1·9	96	2·2	
LSIL	22	0·5	37	0·8	
HSIL or worse	7	0·4	15	0·3	
No cytological result	491	10·0	471	9·7	

BMI, Body mass index; RLU/CO, relative light units/cut-off; ASCUS, atypical squamous cells of undetermined significance; LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion.

Data in this table indicates the number of subjects (*n*) and the percentage of subjects (%) among the enrolled non-drinkers and drinkers.

P values for the categorical and continuous variables were obtained from χ^2 test and *t* test, respectively.

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Table 2. *Odds ratios for persistent infection of high risk-human papillomavirus (HPV)*

Alcohol-related characteristics	Subjects at enrolment *n* (%)	Odds ratios (95% confidence intervals)		
		Enrolment HPV Infection*	1-year follow-up Persistence†	2-year follow-up Persistence†
Alcohol consumption				
Non-drinker	4652 (50·4)	1 (ref.)	1 (ref.)	1 (ref.)
Drinker (former)	390 (4·2)	0·96 (0·68–1·35)‡	1·23 (0·55–2·74)	0·37 (0·05–2·96)
Drinker (current)	4188 (45·4)	1·21 (1·07–1·41)	1·56 (1·09–2·24)	2·49 (1·32–4·71)
Frequency of alcohol consumption				
Non-drinker	4652 (65·8)	1 (ref.)	1 (ref.)	1 (ref.)
Once/month	758 (10·7)	0·85 (0·60–1·21)	1·40 (0·60–3·23)	0·62 (0·08–5·17)
2–4 times/month	806 (11·4)	1·28 (1·04–1·56)	1·64 (0·90–3·02)	2·00 (0·73–5·42)
~2 times/week	855 (12·1)	1·31 (1·04–1·64)	1·80 (1·01–3·36)	1·83 (0·58–5·85)
P value		0·049§	0·603	0·669
Duration of alcohol habit				
<5 years	4870 (62·4)	1 (ref.)	1 (ref.)	1 (ref.)
⩾5 years	2931 (37·6)	1·20 (1·01–1·36)	1·77 (1·19–2·62)	2·33 (1·17–4·63)
Usual amount of beer (200 ml)¶				
Non-drinker	4652 (60·7)	1 (ref.)	1 (ref.)	1 (ref.)
~1 glass	994 (13·0)	1·11 (0·89–1·37)	1·41 (0·80–2·49)	1·31 (0·46–3·72)
2 glasses	1136 (14·8)	1·17 (0·96–1·43)	1·21 (0·71–2·08)	1·12 (0·40–3·13)
~3 glasses	878 (11·5)	1·22 (0·98–1·52)	1·36 (0·75–2·46)	3·62 (1·35–9·75)
P value		<0·001	0·071	0·025
Usual amount of soju (50 ml)‖				
Non drinker	4652 (65·3)	1 (ref.)	1 (ref.)	1 (ref.)
~1 glass	877 (12·3)	1·08 (0·61–1·37)	0·89 (0·31–2·59)	2·16 (0·53–8·83)
2 glasses	897 (12·6)	1·27 (0·96–1·68)	1·68 (0·86–3·27)	2·87 (0·95–8·69)
~3 glasses	703 (9·9)	1·24 (1·03–1·68)	1·11 (0·68–1·81)	0·58 (0·19–1·75)
P value		0·006	0·075	0·786

The subject number for each characteristic is based on the available data rather than all 9230 subjects who answered the indicated questions.

* Enrolment prevalence indicates the HR-HPV infection at the time of enrolment (*vs.* HR-HPV negativity at enrolment).

† 1-year and 2-year HR-HPV persistence were defined as HPV positivity in the 1-year follow-up study year and as HPV positivity in both the 1- and 2-year follow-up study years, respectively, after enrolment with HR-HPV positivity (*vs.* 1- and 2-year HR-HPV negatives defined as HR-HPV negativity for 1 and 2 consecutive years, respectively, after enrolment with HR-HPV negativity).

‡ Odds ratios and 95% confidence intervals were calculated using a multivariate logistic regression analysis (adjusted for age, BMI, marital status, number of children, menopausal status, oral contraceptive use, education level, income level, and smoking status as categorical variables).

§ The *P* value is for the linear trend of multivariate odds ratios (adjusted for age, BMI, marital status, number of children, menopausal status, oral contraceptive use, education level, income level, and smoking status as categorical variables).

¶ Usual amount is defined as the amount of beer or soju (in glasses) normally consumed per occasion.

‖ Soju is a popular alcoholic beverage in Korea with a pure alcohol content (%) about 4–5 times greater than that of beer.

persistence; the OR of current drinkers was 1·56 (95% CI 1·09–2·24) for the risk of 1-year HR-HPV persistence (*vs.* 1-year HR-HPV negative) and 2·49 (95% CI 1·32–4·71) for the risk of 2-year HR-HPV persistence (*vs.* 2-year HR-HPV negative) (Table 2). Drinkers who consumed alcohol ⩾2 times/week had a higher risk of 1-year HR-HPV persistence (OR 1·80, 95% CI 1·01–3·36) than non-drinkers. Drinkers with a ⩾5-year drinking habit had higher risks of 1-year HR-HPV persistence (OR 1·77, 95% CI 1·19–2·62) and 2-year HR-HPV persistence (OR 2·33, 95% CI 1·17–4·63) than women with a <5-year drinking habit. The risk of 2-year HR-HPV persistence showed an increasing trend with more glasses of beer consumed (*P* for trend = 0·025), and in particular, drinkers who consumed ⩾3 glasses of beer had a threefold increased risk of 2-year HR-HPV persistence, compared to non-drinkers (OR 3·62, 95% CI 1·35–9·75).

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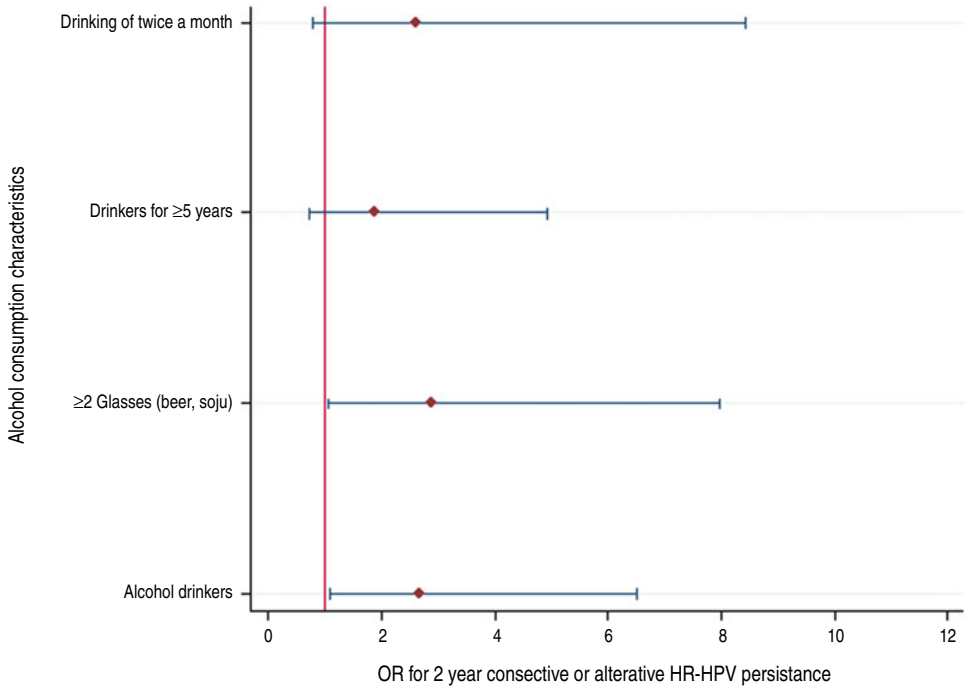

Fig. 1. Odds ratios for 2-year consecutive or alternate high-risk human papillomavirus persistence associated with the characteristics related to alcohol consumption such as 'alcohol drinkers' (non-drinkers *vs.* drinkers); 'usual amount of alcoholic beverages' [2 glasses (50 ml/glass) of beer or soju *vs.* ⩾2 glasses]; 'duration of drinking' (<5 years *vs.* ⩾5 years); and 'frequency of drinking' (<2 times/month *vs.* ⩾2 times/month). A multivariate logistic regression analysis was performed after adjustment for age, body mass index, education level, and the number of children.

Alcohol consumption and 2-year consecutive or alternate HR-HPV persistence

As shown in Figure 1, compared to non-drinkers, the alcohol drinkers had a higher risk of 2-year consecutive or alternate HR-HPV persistence (OR 2·68, 95% CI 1·10–6·51) (*vs.* 2-year consecutive HR-HPV clearance). Women who normally consumed ⩾2 glasses of beer or soju in a single occasion had a higher risk of 2-year consecutive or alternate HR-HPV persistence compared to those who consumed ⩽1 glass of these alcoholic beverages (OR 2·90, 95% CI 1·06–7·98). The drinking duration (⩾5 years) and frequency (⩾2 times/month) demonstrated an increasing trend for the risk although these differences were not significant (OR 1·87, 95% CI 0·71–4·92 and OR 2·60, 95% CI 0·80–8·42, respectively).

DISCUSSION

Our findings demonstrated that alcohol consumption and its associated behaviours, including the frequency of alcohol consumption, duration of drinking habit, and amount of alcoholic beverages consumed increased the risk of 1- and 2-year HR-HPV persistence (*vs.* 1- and 2-year HR-HPV negatives). Alcohol consumption and a high regular consumption of alcoholic beverages increased the risk of 2-year consecutive or alternate HR-HPV persistence (*vs.* 2-year consecutive HR-HPV clearance after enrolment with HR-HPV positivity).

Although alcohol has been reported as a potential risk factor of cervical cancer and HPV infection [2, 13], no studies have investigated the association between specific alcohol behaviours and HPV persistence in the cervix. Our study is the first to demonstrate a significant association between cervical HPV persistence and alcohol consumption. In a few previous studies reporting on epidemic co-factors in natural HPV infection histories, alcohol consumption increased the risk of 36-month HPV infection in college-aged young women, but alcohol was not presented as a risk factor for persistent HPV infections at ⩽6 months [2]. Goodman *et al.* reported that cervical HPV acquisition increased with alcohol consumption among sexually active multi-ethnic women, aged 18–85

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years, who were recruited from Hawaii, but cervical HPV clearance did not correlate with alcohol consumption [13]. In contrast to the lack of studies on alcohol and HPV persistence, several cervical cancer cohort studies have been conducted with respect to alcoholics or alcoholism [15–17]. A single large-scale population-based cohort study assessed the association between moderate alcohol intake and the total incidence of cancer among women in the UK, but no significant association was found with cervical cancer [18].

A critical point is that the drinkers in our cohort had a light-to-moderate level of alcohol consumption; the mean daily alcohol amount consumed by the drinkers (6·0 ± 9·5 g/day) was within the range of light-to-moderate alcohol consumption for Korean women (1·0–14·9 g/day [19]). Additionally, drinking of beer, a mild type of alcohol (the rates of pure alcohol in beer and soju are 4·5% and 21%, respectively) showed the highest risk of HPV persistence with a regular consumption of ⩾3 glasses of beer. Daily alcohol consumption had a relatively high level in our subjects, but this is included in a moderate alcohol consumption level. The benefits of moderate alcohol consumption have been suggested by several health outcomes, but to date, controversies and inconsistent findings exist [20]. As reported in a recent meta-analysis that investigated the relationship between alcohol consumption and the mortality risk of all cancers, a J-shaped association was found in men but not in women [21]. In a large-scale prospective study of Korean men and women, light-to-moderate alcohol consumption was associated with lower mortality risks from all causes and from cancer in men, but did not show favourable effects on the risks in women [19]. Members of Asian populations frequently present with a slow-metabolizing acetaldehyde dehydrogenase variant [22]. Furthermore, there are gender differences in alcohol pharmacokinetics and alcohol-related comorbidities [23]. Therefore, the genetic susceptibility of Asian women to alcohol might differ from that of other populations with respect to defence against viral infection or viral clearance.

There are potential direct mechanisms to support a positive association between alcohol and HPV persistence. Alcohol can induce folate deficiency by reducing the absorption of folate in the colon and thus induce DNA hypomethylation [24]. In fact, folate is a plausible protective factor against cervical cancer [25] and high levels have potential effects against the initiation of HPV-related dysplasia [26, 27]. Additionally, alcohol activates cytochrome P450 2E1 which leads to the production of reactive oxygen species (ROS) [28], and various antioxidant enzymes and detoxifying pathways are consistently associated with HPV-transformed cells [29]. As reported in several studies, cervical ROS could contribute to a divergent host response against the viral infection because of highly variable concentrations of amines and amine oxidases in the cervical mucus [30]. Moreover, women with high ferritin levels were less likely to clear HR-HPV due to the increased generation of ROS than those with lower levels [31]. The immune system is important in viral disease, but the mechanisms that influence specific host immunity against HPV remain unclear [32].

In our study, the frequency of current drinkers in the subjects (45·4%) was higher than the overall frequency of drinkers (20·3%) among Korean women [19]. The reason for the higher rate of light-to-moderate alcohol drinkers in this study might be the higher socioeconomic status of our subjects, as determined by factors such as household income. Compared to the mean monthly household income in Korea (about 199 and 386 million won in 2001 and 2011, respectively) [33], our subjects had a higher income level (about 390 million won). It is a known fact that lower socioeconomic groups are at a higher risk of binge- or heavy drinking, while higher socioeconomic groups are associated with a higher frequency of light drinking [34, 35]. Furthermore, the drinkers in our subject cohort were characterized as younger, more likely to smoke, and more likely to use oral contraceptives compared to non-drinkers. Although a regression analysis was performed after sufficiently adjusting for these characteristics, undisclosed social factors of the moderate drinkers or the complex natures of these factors could influence the risk of HPV persistence.

This study has some limitations. Sexual activity could not be considered as a confounding factor for HPV infection because of the absence of sexual behaviour-related questions in the health screening questionnaire. The mean age of our study subjects was 48 years (⩾40 years: 81%). A reduced sexual interest and desire along with a reduced frequency of sexual intercourse have been reported among middle-aged women [36]. About 89% and 71% of Korean women aged 40–49 and 50–59 years, respectively, reported having an inactive sexual life and the highest sexual intercourse frequency was once/month in those aged 40–49 years [37]. However, the incidence of cervical cancers in Korea was highest in

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middle-aged women (35–64 years). Sexual behaviours in this population might not greatly affect the association found in the study. Second, persistent HPV infection was defined according to the HC-II HPV genotype pooling method rather than HPV genotype-specific detection. However, it was reported that 1-year HPV persistence as detected by HC-II is more sensitive and predictive for CIN-3 than determination of genotype-specific persistence by linear blot assay [38, 39]. The pooled detection of multiple oncogenic HPV genotypes can also minimize false-negative errors [39]. Furthermore, about 86·3% of Korean women had one or two sexual partners in their lifetimes [40, 41] and 91·3% did not report having new sexual partners in the past 6 months [41]. Persistent HPV infection with the same genotype is highly probable.

In conclusion, this study demonstrates that light-to-moderate alcohol consumption or related behaviours may increase the risk of cervical HR-HPV persistence and infection. These increases may be caused by the direct harmful effects of alcohol on the cervix, or the combination of alcohol consumption, and the social behaviours of female moderate drinkers. We suggest that more studies that investigate the correlation between moderate alcohol consumption and HR-HPV persistence should be performed, particularly in Korean women.

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DECLARATION OF INTEREST

None.

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