Relationship between circumcision and human papillomavirus infection: a systematic review and meta-analysis

Yi-Ping Zhu¹², Zhong-Wei Jia¹², Bo Dai¹², Ding-Wei Ye¹², Yun-Yi Kong¹³, Kun Chang¹², Yue Wang¹²

Male circumcision (MC) is reported to reduce human papillomavirus (HPV) prevalence in men. However, the efficacy remains imprecise. The aim of this study was to conduct a systematic review and meta-analysis to assess the relationship between MC and genital HPV infection and genital warts. PUBMED, EMBASE, and Web of Science were searched from inception to March 22, 2015. We identified 30 papers, including a total of 12149 circumcised and 12252 uncircumcised men who were evaluated for the association of circumcision with genital HPV or genital warts. Compared with men who were not circumcised, circumcised men may have had significantly reduced odds of genital HPV prevalence (odds ratio [OR]: 0.68; 95% confidence interval [95% CI]: 0.56–0.82). There was no significant association between MC and genital HPV acquisition of new infections (OR: 0.99; 95% CI: 0.62–1.60), genital HPV clearance (OR: 1.38; 95% CI: 0.96–1.97), and prevalence of genital warts (OR: 1.17; 95% CI: 0.63–2.17). This meta-analysis suggests that circumcision reduces the prevalence of genital HPV infections. However, no clear evidence was found that circumcision was associated with decreased HPV acquisition, increased HPV clearance, or decreased the prevalence of genital warts. More studies are required to evaluate adequately the effect of MC on the acquisition and clearance of HPV infections and prevalence of genital warts.

Asian Journal of Andrology (2017) 19, 125–131; doi: 10.4103/1008-682X.175092; published online: 8 March 2016

Keywords: genital warts; human papillomavirus; male circumcision; prevalence

INTRODUCTION

Human papillomavirus (HPV) infection is common and can cause genital warts, invasive cervical cancer in women, and penile and anal cancer in men.¹ Cervical cancer is the second most common cancer among women worldwide. Up to 99% of cervical cancers are associated with infection of oncogenic HPV genotypes.² Therefore, finding interventions that can reduce the risk of HPV infection may have a protective impact on HPV-related diseases, both in men and women.

Male circumcision (MC) is a simple, rapid operation; however, it remains unclear whether it has a protective effect against genital HPV infection. A systematic review of studies conducted by Van Howe et al.³ found no evidence of an association between MC and genital HPV infections. However, two meta-analyses⁴,⁵ and several studies⁶–⁸ found that MC could help reduce HPV infections. Recently, a randomized controlled trial (RCT) with a large patient population demonstrated that MC was not associated with the acquisition and clearance of genital HPV infection.⁹ Based on the discrepancy between these findings, there is an urgent need to perform an updated meta-analysis on this topic. In the present systematic review and meta-analysis, we added five recent papers¹⁰–¹² (including 4103 circumcised and 5916 uncircumcised men) to provide a comprehensive survey to address this controversy.

MATERIALS AND METHODS

Data sources and search strategy

PUBMED, EMBASE, and Web of Science were searched from inception until March 22, 2015. The search was performed using the following terms: “circumcision, male,” “HPV,” “papillomaviridae,” “genital diseases,” “male,” “genital warts,” and “condylomata acuminata.” We also examined the reference lists of all relevant papers. The criteria for eligibility were as follows: (1) evaluate the potential association between MC and HPV infection or MC and genital warts; (2) give a precise description about how MC status was ascertained; and (3) reporting of HPV sampling techniques, sampling sites, and details of the different polymerase chain reaction assays used for HPV DNA detection. We excluded studies if they (1) did not report any of the outcomes of interest, (2) enrolled men who were HIV-positive, (3) had interventions that did not include MC, and (4) contained data that could not be extracted in an appropriate format and any attempts to obtain the relevant data from the authors had failed.

Data extraction and quality assessment

We systematically assessed the quality of all the studies included. Data were extracted independently by two authors (YP-Z and ZW-J) and disagreements were discussed to reach consensus between the two authors or consultation with a third reviewer. We classified as separate studies...
if more than one outcome (HPV prevalence, HPV acquisition, HPV clearance, and genital warts) was evaluated in one paper. The following data were extracted from the studies: (1) publication details, including first author and year of publication; (2) study design; (3) characteristics of the studied population, including sample size, age range, study population, and country in which the study was conducted; (4) method of ascertaining MC status (self-reported or physical examination); (5) the proportion of circumcised and uncircumcised men; and (6) positive events among circumcised and uncircumcised men.

Statistical analysis

Review Manager version 5.2 software (Cochrane Collaborative, Oxford, UK) was used to integrate all of the individual outcomes. Heterogeneity among the studies was measured by a random-effects model using the $\chi^2$ test, $P$ values, and $I^2$ statistics. $P < 0.05$ was considered statistically significant. Publication bias was estimated by the funnel plot and Begg's rank regression test using STATA version 12.0 software (Stata Corporation, College Station, TX, USA). $P < 0.1$ was considered statistically significant publication bias.

RESULTS

Data retrieval

A total of 5082 citations were identified after the initial database search. After reading the titles and abstracts, 78 papers were retrieved. Fifty-four of these papers were excluded after full-text review. In addition, seven papers were retrieved from the reference lists of all relevant papers. Thus, 30 papers (39 studies) involving a total of 12 149 circumcised and 12 252 uncircumcised men were finally included in this meta-analysis (Figure 1).

Study characteristics

The characteristics of patients enrolled in our meta-analysis are summarized in Tables 1–3. Twenty-four studies evaluated the association between MC and HPV prevalence; six evaluated the association between MC and HPV acquisition; four evaluated the association between MC and HPV clearance; and five evaluated the association between MC and genital warts.

HPV specimens were collected from different regions including glans, penile shaft, coronal sulcus, scrotum, foreskin, urethra, and perianal region. All studies measured HPV DNA by polymerase chain reaction. The sampling method and specimen collection sites of studies about MC and HPV prevalence are summarized in Table 4.

MC and HPV prevalence

Twenty-four studies evaluated the association between MC and HPV prevalence (Table 1). The random-effects model was applied to calculate the pooled odds ratio (OR) and its 95% CI. HPV-positive rates among circumcised and uncircumcised men ranged from 2.4% to 78.0% and 7.0% to 81.2%, respectively. HPV prevalence was lower in circumcised than in uncircumcised men in 10 of the 24 studies but higher in one study. In addition, 13 studies showed MC had no effect on HPV prevalence. In general, MC significantly reduced the odds of genital HPV prevalence (OR: 0.68; 95% CI: 0.56–0.82), but substantial between-study heterogeneity was observed ($I^2 = 70\%$) (Figure 2).

MC and HPV acquisition

Five cohort studies and one RCT examined the effect of MC on genital HPV acquisition (Table 2). HPV acquisition was defined as follows: a new infection identified in men who were initially negative for any HPV and who acquired one or two or more new HPV infections during the next follow-up or men who were initially positive for a specific HPV genotype but acquired one or more new HPV genotypes during the next follow-up. The proportion of men who were circumcised ranged from 17.1% to 87.7%. The interval of follow-up ranged from 12 to 24 months. The proportion of HPV acquisition among circumcised and uncircumcised men ranged from 15.7% to 62.6% and 21.3% to 66.2%, respectively. In general, there was no significant association between MC and genital HPV acquisition (OR: 0.99; 95% CI: 0.62–1.60). Substantial heterogeneity was observed among the studies ($I^2 = 87\%$) (Figure 3).

MC and HPV clearance

Three cohort studies and one RCT examined the effect of MC on genital HPV clearance (Table 2). Clearance was defined as the proportion of men with preexisting HPV, who were negative for that genotype at a subsequent sequential study visit. The study population ranged from 105 to 4033. The proportion of men who were circumcised ranged from 7.6% to 87.7%. The interval of follow-up ranged from 12 to 24 months. The proportion of HPV clearance among circumcised and uncircumcised men ranged from 31.2% to 100% and 25.7% to 72.8%, respectively. In general, there was no significant association between MC and genital HPV clearance (OR: 1.38; 95% CI: 0.96–1.97). Substantial heterogeneity was observed among the studies ($I^2 = 56\%$) (Figure 4).

MC and genital warts

Three cross-sectional two case–control studies examined the effect of MC on genital warts (Table 3). The study population was men attending sexually transmitted disease (STD) clinics, general population, or partners of women with cervical intraepithelial neoplasia. Three studies assessed current warts and two assessed historic warts. The proportion of men who were circumcised ranged from 4.0% to 83.5%. In general, there was no significant association between MC and genital warts (OR: 1.17; 95% CI: 0.63–2.17). Substantial heterogeneity was observed among the studies ($I^2 = 68\%$) (Figure 5).

Publication bias

Begg's funnel plot and Egger's test were performed to assess the publication bias of studies on HPV prevalence. The funnel plots did
Table 1: Summary of studies reporting on the association between MC and HPV prevalence in men

| Study                  | Country                              | Design          | Study population                                      | Age     | Study size | Male circumcision assessment | Male circumcision assessment |
|------------------------|--------------------------------------|-----------------|------------------------------------------------------|---------|------------|------------------------------|----------------------------|
| Aynaud et al. 2002     | France                               | Cross-sectional| Partners of women with HPV-associated genital lesions| 19–42   | 111        | Physical examination         |                             |
| Castelisague et al. 2002 | Brazil, Colombia, Thailand, Philippines, and Spain | Pooled data-case-control | Husbands/stable partners of women with or without cervical cancer | 37–57   | 1139       | Physical examination         |                             |
| Sware et al. 2002      | Denmark                              | Cross-sectional| STD clinics patients                                  | 18–40   | 198        | Self-reported                |                             |
| Shin et al. 2004       | South Korea                          | Cross-sectional| University students                                   | 18–28   | 368        | Self-reported                |                             |
| Weaver et al. 2004     | The USA                              | Cross-sectional| Undergraduate students                                | 18–25   | 279        | Physical examination         |                             |
| Baldwin et al. 2004    | The USA                              | Cross-sectional| STI clinic attendees (high risk)                      | 18–70   | 344        | Physical examination         |                             |
| Bleecker et al. 2005   | The Netherlands                      | Cross-sectional| Partners of women with CIN                            | -       | 224        | Clinical exam                |                             |
| Lajous et al. 2005     | Mexico                               | Cohort          | Healthy military men                                  | 16–40   | 925        | Self-reported                |                             |
| Vaccarella et al. 2006 | Mexico                               | Cross-sectional| Men who requested a vasectomy in public clinics       | 25–45   | 779        | Physical examination         |                             |
| Rombaldi et al. 2006   | Brazil                               | Cross-sectional| Partners of women with CIN                            | -       | 99         | Not reported                 |                             |
| Partridge et al. 2007  | The USA                              | Cohort          | Male university students                               | 18–20   | 239        | Physical examination         |                             |
| Hernandez et al. 2008  | The USA                              | Cohort          | University population, primarily heterosexual adult males | 18–79   | 254        | Physical examination         |                             |
| Nielson et al. 2007    | The USA                              | Cross-sectional| General population volunteers and STD clinic attendees | 18–40   | 463        | Physical examination         |                             |
| Ng’ayo et al. 2008     | Africa                               | Cross-sectional| Men worked in the fishing industry                    | 18–63   | 250        | Physical examination         |                             |
| Lu et al. 2009         | The USA                              | Cohort          | General population                                     | 18–44   | 285        | Physical examination         |                             |
| Giuliano et al. 2009   | Brazil, Mexico, and the USA          | Cohort          | General population, universities, and organized health care systems (Mexico only) | 18–70   | 988        | Physical examination         |                             |
| Ogilvie et al. 2009    | Canada                               | Cross-sectional| STD clinics patients                                  | 16–69   | 262        | Physical examination         |                             |
| Muller et al. 2010     | South Africa                         | Cross-sectional| Sexual health clinic attendees, HIV prevalence 49.5%  | -       | 208        | Physical examination         |                             |
| Tobias et al. 2009     | Africa                               | RCT             | HIV-negative, uncircumcised male subjects              | 15–49   | 520        | Physical examination         |                             |
| Auvert et al. 2009     | Africa                               | RCT             | General population of uncircumcised men               | 18–24   | 1264       | Physical examination         |                             |
| Vanbuskirk et al. 2011 | Washington                          | Cohort          | Male University of Washington students                | 18–20   | 477        | Physical examination         |                             |
| Tobias et al. 2011     | Rakai, Uganda                        | RCT             | General population                                     | 15–49   | 459        | Immediate circumcision       |                             |
| Tarnaud et al. 2011    | South Africa                         | RCT             | General population                                     | 18–24   | 1573       | Physical examination         |                             |
| Backes et al. 2012     | Kenya                                | RCT             | Participants were recruited from STI clinics, workplaces, and community organizations | 18–24   | 275        | Physical examination         |                             |

MC: male circumcision; HPV: human papillomavirus; STD: sexually transmitted disease; STI: sexually transmitted infection; CIN: cervical intraepithelial neoplasia; RCT: randomized controlled trial

Table 2: Summary of studies reporting on the association between MC and HPV acquisition and HPV clearance in men

| Study                  | Country                              | Design          | Study population                                      | Age     | Study size | Male circumcision assessment | HPV acquisition | HPV clearance |
|------------------------|--------------------------------------|-----------------|------------------------------------------------------|---------|------------|------------------------------|----------------|--------------|
| Lajous et al. 2005     | Mexico                               | Cohort          | Healthy military men                                  | 16–40   | 210        | Self-reported                | 105            |              |
| Partridge et al. 2007  | The USA                              | Cohort          | Male university students                               | 18–20   | 240        | Physical examination         | N/A            |              |
| Lu et al. 2009         | The USA                              | Cohort          | General population residents of southern Arizona      | 18–44   | 285        | Physical examination         | 285            |              |
| Gray et al. 2010       | Rakai, Uganda                        | RCT             | HIV-uninfected men                                     | 15–49   | 840        | Physical examination         | 645            |              |
| Vanbuskirk et al. 2011 | Washington                          | Cohort          | Male University of Washington students                | 18–20   | 477        | Physical examination         | N/A            |              |
| Albero et al. 2014     | Brazil, Mexico, and the USA          | Cohort          | General population, universities, and organized health-care systems | 18–70   | 4033       | Physical examination         | 4033           |              |

N/A: not applicable; RCT: randomized controlled trial; MC: male circumcision; HPV: human papillomavirus

Table 3: Summary of studies reporting on the association between MC and genital warts in men

| Study                  | Country                              | Design          | Study population                                      | Age     | Circumcised (%) | Study size | Male circumcision assessment |
|------------------------|--------------------------------------|-----------------|------------------------------------------------------|---------|----------------|------------|------------------------------|
| Cook et al. 1994       | The USA                              | Cross-sectional| STI clinic attendees                                  | N/A     | 2236           | 2776       | Physical examination         |
| Donovan et al. 1994    | Australia                            | Cross-sectional| STI clinic attendees                                  | N/A     | 185            | 300        | Physical examination         |
| Van Den Eeden et al. 1998 | The USA                        | Case-control    | General population                                     | N/A     | 198            | 237        | Self-reported                |
| Tseng et al. 2001      | The USA                              | Case-control    | General population                                     | <75     | 43             | 100        | Physical examination         |
| Bleecker et al. 2005   | The Netherlands                      | Cross-sectional| Partners of women with CIN                            | N/A     | 9              | 224        | Clinical exam                |

N/A: not applicable; MC: male circumcision; STI: sexually transmitted infection; CIN: cervical intraepithelial neoplasia

not reveal any evidence of obvious asymmetry among the 24 studies included (Figure 6). Egger’s test was used to provide statistical evidence of funnel plot symmetry. The results still did not suggest any evidence of publication bias (P = 0.271).
Table 4: Summary of studies reporting on the association between MC and genital HPV Prevalence in men by sampling method and specimen collection sites

| Study                  | Sampling methods | HPV DNA detection assay | Specimen collection sites included |
|------------------------|------------------|-------------------------|-----------------------------------|
|                        |                  |                         | Urethra meatus | Gland | Coronal sulcus | Foreskin | Penile shaft | Scrotum | Perianal region | Semen |
| Aynaud et al. 200220   | Unknown          | Unknown                 | –           | –     | –             | –        | –            | –       | –                 | +     |
| Castellsague et al. 200223 | Swabs            | PCR MY09/11             | +           | +     | –             | –        | –            | –       | –                 | –     |
| Sware et al. 200214    | Swabs            | PCR GP5+/6+             | –           | +     | +             | +        | –            | –       | –                 | –     |
| Shin et al. 200421     | Cytobrush        | PCR SPF10               | +           | +     | +             | –        | –            | –       | –                 | –     |
| Weaver et al. 20044    | Emery paper and swabs | PCR PGMY09/11         | +           | +     | –             | +        | +            | –       | –                 | –     |
| Baldwin et al. 200422  | Swabs            | PCR PGMY09/11           | –           | –     | +             | –        | –            | –       | –                 | –     |
| Bleeker et al. 20057   | Brush            | PCR GP5+/6+             | –           | +     | +             | –        | –            | –       | –                 | –     |
| Lajous et al. 200523   | Swabs cytobrush  | PCR PGMY09/11           | +           | –     | +             | –        | –            | –       | –                 | –     |
| Vaccarella et al. 200664 | Cytobrush        | PCR PGMY09/11           | +           | +     | +             | +        | –            | –       | –                 | –     |
| Romboldi et al. 200614 | Brush            | PCR PGMY09/11           | +           | –     | +             | +        | –            | –       | –                 | –     |
| Partridge et al. 200715 | Emery paper and swabs | PCR PGMY09/11         | +           | +     | –             | +        | +            | –       | –                 | –     |
| Hernandez et al. 200827 | Textured paper and swabs | PCR PGMY09/11        | –           | –     | +             | +        | +            | –       | –                 | –     |
| Nielson et al. 200725  | Swabs            | PCR PGMY09/11           | +           | +     | +             | +        | –            | –       | –                 | –     |
| Ng’ayo et al. 200826   | Swabs            | PCR PGMY09/11           | +           | +     | +             | –        | –            | –       | –                 | –     |
| Lu et al. 200916       | Swabs            | PCR PGMY09/11           | –           | +     | +             | +        | –            | –       | –                 | –     |
| Giuliano et al. 200928 | Swabs            | PCR GMY09/11            | –           | +     | +             | +        | –            | +       | –                 | –     |
| Orlivie et al. 20099    | Emery paper and swabs | PCR Roche Amplicor HPV test | –       | +     | +             | +        | –            | +       | –                 | –     |
| Muller et al. 201010    | Swabs            | LA HPV genotyping test  | –           | –     | +             | –        | –            | +       | –                 | –     |
| Tobian et al. 200930   | Swabs            | PCR GMY09/11            | –           | –     | +             | +        | –            | –       | –                 | –     |
| Auvert et al. 20094    | Swabs            | PCR Roche Amplicor HPV test | +       | +     | –             | –        | –            | –       | –                 | –     |
| Vanbuskirk et al. 201110 | Swabs            | PCR PGMY09/11           | +           | +     | +             | –        | –            | –       | –                 | –     |
| Tobian et al. 20111    | Swabs            | Roche HPV LA            | –           | –     | +             | –        | –            | –       | –                 | –     |
| Tarnaud et al. 201111   | Swabs            | HPV LA                  | +           | –     | –             | –        | –            | –       | –                 | –     |
| Backes et al. 201212   | Swabs            | PCR GP5+/6+             | –           | +     | +             | –        | –            | –       | –                 | –     |

PCR: polymerase chain reaction; MC: male circumcision; HPV: human papillomavirus; LA: linear array

Figure 2: Forest plot of the studies assessing the association between MC and HPV prevalence. MC: male circumcision; HPV: human papillomavirus.
DISCUSSION

The existing evidence, which includes data from case–control, cross-sectional and cohort studies, and RCTs, was analyzed in our meta-analysis to ascertain pooled estimates of the relationship between MC and genital HPV prevalence. Overall, our results revealed that MC reduced the prevalence of genital HPV infection in an average of 32% of men. This means that there is a need to perform three circumcisions to prevent one infection. While a series of studies and our meta-analysis demonstrated an inverse association between MC and HPV prevalence in men, one meta-analysis conducted in September 2006 revealed that there was no significant association between circumcision status and HPV prevalence.

Because HPV is a topical infection in the skin and mucosa, one possible explanation for the discrepancy may be the varied specimen collection sites in the different studies. HPV detection varies by anatomical site and evaluating HPV only on the coronal sulcus and urethra might bias the estimated protective efficacy of MC. More frequent HPV infection was detected on the coronal sulcus than the shaft in uncircumcised men, suggesting that the moist preputial space might provide a more favorable environment for HPV infection. When interpreting the effect of different sampling methods on our results, we should note that the effectiveness of sampling methods at different anatomical sites and the sampling method itself may affect the efficacy of the sampling methods. However, it is impossible to make a comment on those effects; thus, the method used to sample HPV may be a source of heterogeneity.

Only a few studies assessed the association between MC and HPV acquisition or clearance. The present meta-analysis suggests no evidence of an effect of decreased HPV acquisition (OR: 0.99; 95% CI: 0.62–1.60) and increased HPV clearance (OR: 1.38; 95% CI: 0.96–1.97). However, one RCT conducted in Uganda and a cohort study in the USA found that MC reduced acquisition of HPV infection. On the contrary, one recently published cohort study which enrolled 4033 healthy men and three observational prospective studies suggested that MC was not associated with an overall reduction of genital HPV acquisition, which was consistent with our findings. Although limited data prevented us from performing a subgroup analysis according to sample sites, only a few studies used specimens collected from the scrotum, perianal area, and semen, which might have resulted in selection bias in our meta-analysis. In addition, our results suggested that there was no evidence of MC increasing HPV.
clearance (OR: 1.38; 95% CI: 0.96–1.97). When interpreting the results of our meta-analysis, we must note that HPV has a high rate of spontaneous clearance, and we suggest that the sampling sites also played an important role in the final results. One RCT suggested that MC increased HPV clearance when sampled on the coronal sulcus.** However, when sampled on the scrotum and penile shaft, Hernandez et al.** found that HPV clearance was not affected by MC. In addition, when interpreting the differences in findings between reduced prevalence of HPV after MC and no reduction in acquisition or increased clearance after MC, we suggest that this might have been because the study population for HPV acquisition and clearance was smaller than for HPV prevalence. Therefore, the results need to be validated using a larger number of studies.

Our meta-analysis suggested that there was no significant association between MC and genital warts (OR: 1.17; 95% CI: 0.63–2.17). One study suggested that genital warts were more likely at distal lesions on the penis among uncircumcised men. Another study suggested that uncircumcised men were more likely to present with extensive warts. In contrast, one prospective cohort study conducted in Kenya suggested that the risk of genital warts was not affected by MC. As we only found five papers suitable for our meta-analysis, additional studies are necessary to investigate the relationship between MC and genital warts.

It is plausible that MC might reduce genital HPV infection; however, the mechanism is unclear. In uncircumcised men, the inner preputial mucosa is exposed to vaginal and cervical secretions as the foreskin is retracted during intercourse. The penile shaft and surface of the foreskin are covered by a keratinized stratified squamous epithelium that could provide a protective effect against HPV infection. However, the foreskin mucosa is not keratinized and might be more susceptible to HPV infections. In addition, the moist environment of the foreskin may provide a favorable condition for HPV survival. It has been proposed that keratinization of the circumcision scar may also reduce the chance of HPV infection. Therefore, MC may reduce the chance of HPV access to epidermal basal cells.

Our meta-analysis included five additional papers that were not included in the most recent systematic review about MC and genital HPV infection. At the same time, we enrolled an additional 4103 circumcised and 5916 uncircumcised men to provide a comprehensive survey about the relationship between MC and genital HPV infection. As the results of previous meta-analyses and several other studies showed major differences, it is urgent that an agreement is reached. Even though our results are consistent with the recent two meta-analyses, our meta-analysis validated the results through using a larger sample size. Compared to the recent two meta-analyses, to reduce the heterogeneity among the enrolled studies, enrollment in our meta-analysis were restricted to HIV-negative men, and one RCT conducted among HIV-positive men was excluded.

Our meta-analysis had several limitations. First, there was considerable heterogeneity among the studies. This was because of different study types (case–control, cross-sectional, cohort, and RCT), patients coming from different regions, and differences in results between the normal population (lower risk) and those attending sexually transmitted disease (STD) clinics or partners of HPV-infected women (higher risk). It was not possible to run a subset analysis with the existing data; therefore, these factors might have influenced our results. Second, sampling methods and specimen collection sites varied considerably among the included studies. Third, some of the studies were observational, the MC status was ascertained by self-report, and it was hard to give an accurate assessment of the effect of the surgical procedure. At the same time, age at circumcision and different surgical methods may also have affected our results. Finally, our results for HPV acquisition and clearance could have been influenced by a single study providing two-thirds of all the patients and this may have introduced bias to the overall results.

HPV infection has been established as an important cause of invasive cervical cancer in women and penile cancer in men. Our results suggested that MC could reduce the odds of genital HPV prevalence. MC as a useful intervention could reduce the risk of HPV infection in men and may also have a preventive impact on HPV-related diseases both in men and women.

CONCLUSIONS

This meta-analysis suggested that MC was strongly associated with reduced odds of genital HPV prevalence. MC as a useful intervention could reduce the risk of HPV infection should be advocated, especially in countries where HPV vaccines are not yet available.

AUTHOR CONTRIBUTIONS

YPZ and ZWJ designed the study, collected the clinical data, and drafted the manuscript. BD and DWY supervised and revised the manuscript. YYK analyzed some of the data. KC and YW performed the literature search and selected the studies. All authors reviewed and approved the manuscript.

COMPETING INTERESTS

All authors declared no competing interests.

ACKNOWLEDGMENTS

This study was supported by a grant from the International Cooperation and Exchange of Science and Technology Commission of Shanghai Municipality (No. 12410709300), a grant from the Guide Project of Science and Technology Commission of Shanghai Municipality (No. 124119a7300) and a grant from the Outstanding Young Talent Training Plan of Shanghai Municipal Commission of Health and Family Planning (No. XYQ2013102).

REFERENCES

1. Tobian AA, Keng X, Gravitt PE, Eaton KP, Kigozi G, et al. Male circumcision and anatomic sites of penile high-risk human papillomavirus in Rakai, Uganda. Int J Cancer 2011; 129: 2970–5.
2. Bosch FX, Shai KV, Manos MM, Munoz N, Sherman M, et al. Prevalence of human...
Asian Journal of Andrology

Prevalence and determinants of genital infection with human papillomavirus, in female and male university students in Busan, South Korea. J Infect Dis 2004; 190: 468–76.

Baldwin SB, Wallace DR, Papenfuss MR, Abrahamsen M, Vaught LC. Condom use and other factors affecting penile human papillomavirus detection in men attending a sexually transmitted disease clinic. Sex Transm Dis 2004; 31: 601–7.

Lajous M, Mueller N, Cruz-Valdez A, Aguilar LV, Franceschi S, et al. Determinants of prevalence, acquisition, and persistence of human papillomavirus in healthy Mexican military men. Cancer Epidemi Biomarkers 2005; 14: 1710–6.

Vaccarella S, Lazcano-Ponce E, Castro-Garduño JA, Cruz-Valdez A, Díaz V, et al. Prevalence and determinants of human papillomavirus infection in men attending vasectomy clinics in Mexico. Int J Cancer 2006; 119: 1934–9.

Nielsen CM, Flores R, Harris RB, Abrahamsen M, Papenfuss MR, et al. Human papillomavirus prevalence and type distribution in male anogenital sites and semen. Cancer Epidemi Biomarkers 2007; 16: 1107–14.

Ng’Ayo MO, Bukusi E, Rowhani-Rahbar A, Koutsy LA, Feng Q, et al. Epidemiology of human papillomavirus infection among fishermen along Lake Victoria Shore in the Kisumu District, Kenya. Sex Transm Infect 2008; 84: 62–6.

Hernandez BY, Wiikens LR, Zhu X, McDuffie K, Thompson P, et al. Circumcision and human papillomavirus infection in men: a site-specific comparison. J Infect Dis 2008; 197: 787–94.

Giuliano AR, Lazcano E, Villa LL, Flores R, Salmeron J, et al. Circumcision and sexual behavior: factors independently associated with human papillomavirus detection among men in the HIM study. Int J Cancer 2009; 124: 1251–7.

Ogilvie GS, Taylor DL, Achen M, Cook D, Krajden M. Self-collection of genital human papillomavirus specimens in heterosexual men. Sex Transm Infect 2009; 85: 221–5.

Tobian AA, Serwadda D, Quinn TC, Kigozi G, Gravitt PE, et al. Male circumcision for the prevention of HSV-2 and HPV infections and syphilis. New Engl J Med 2009; 360: 1298–309.

Muller EE, Chirwa TF, Lewis DA. Human papillomavirus (HPV) infection in heterosexual African men attending sexual health services: associations between HPV and HIV serostatus. Sex Transm Infect 2010; 86: 175–80.

Gray RH, Serwadda D, Kong X, Makumbi F, Kigozi G, et al. Male circumcision decreases acquisition and increases clearance of high-risk human papillomavirus in HIV-negative men: a randomized trial in Rakai, Uganda. J Infect Dis 2010; 201: 1455–62.

Cook LS, Koutsy LA, Holmes KK. Circumcision and sexually transmitted diseases. Am J Public Health 1994; 84: 197–201.

Van Den Eeden SK, Habel LA, Sherman KJ, McKnight B, Stergachis A. Risk factors for incident and recurrent condylomata acuminate among men. A population-based study. Sex Transm Dis 1996; 23: 278–84.

Tseng H, Morgenstern H, Mack T, Peters RK. Risk factors for penile cancer: results of a population-based case-control study in Los Angeles County (United States). Cancer Cause Control 2001; 12: 267–77.

Oriel JD. Natural history of genital warts. Br J Vener Dis 1971; 47: 1–13.

Lavery L, Rakwar JP, Thompson ML, Jackson DJ, Mandalaya K, et al. Effect of circumcision on incidence of human immunodeficiency virus type 1 and other sexually transmitted diseases: a prospective cohort study of trucking company employees in Kenya. J Infect Dis 1999; 180: 330–6.

Serwadda D, Wawer MJ, Makumbi F, Kong X, Kigozi G, et al. Circumcision of HIV-infected men: effects on high-risk human papillomavirus infections in a randomized trial in Rakai, Uganda. J Infect Dis 2010; 201: 1463–9.

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.