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Editorial

Human papillomavirus testing as a primary screening tool for cervical cancer

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Since the 1940s, cytology-based cervical cancer screening has been widely used for cancer control and has led to a significant reduction in the incidence of cervical cancer. Despite these effective screening tools, however, more than 500,000 women are diagnosed with cervical cancer, and 300,000 women die from this disease globally every year [1]. Screening for human papillomavirus (HPV), as the main cause of cervical cancer, was introduced in the 1990s and has become an effective screening tool for cervical cancer in many countries. Evidence from randomized controlled trials (RCTs) suggests that screening with high-risk HPV (hrHPV) is more sensitive than cytological screening methods to detect cervical precancerous lesions [2]. The United States Food and Drug Administration approved the Cobas HPV DNA test (Roche Diagnostics, Basel, Switzerland) for primary cervical cancer screening in 2014. Subsequently, the United States Preventive Services Task Force recommended screening for hrHPV alone once every 5 years as a preferred strategy in 2018 [3]. Moreover, HPV testing may be a more important screening method for cervical cancer after implementation of HPV vaccination [4].

However, previous studies have mainly been conducted in Europe and, to our knowledge, there have been no studies involving Asian populations. Therefore, the study by Kono et al. [5] is particularly meaningful in that it evaluated its utility as a primary screening test for hrHPV test compared with cytology in Asians. This population cohort study compared cytology versus cytology + hrHPV tests in 25,000 Japanese women. It revealed the real-world impact of cervical screening programs that implemented HPV testing. However, a regrettable aspect of this study was that there was no randomization or clear standard for dividing the intervention and control groups to prevent unbalanced group assignment [6].

In this study, if the hrHPV test was added to cytology, approximately 5.8% of patients underwent additional colposcopy, thus increasing the referral rate. Although this result may be due to unbalanced group assignment as a product of the study design, it suggested that higher false-positive rate and colposcopy referral rate of primary HPV screening and co-testing compared with cytology may be a barrier to adaptation of this approach. However, a relatively high referral rate could be temporary in the first round. In the HPV FOCAL RCT, colposcopy referral rates (reported as rate per 1,000) in the intervention group were significantly higher in round 1 (intervention, 57.0 [95% confidence interval; CI=52.5–61.9] vs.

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control, 30.8 [95% CI=27.5–34.5]) [7]. However, after 48 months, the referral rates were lower in the intervention group than in the control group for all ages (49.2 [95% CI=45.0–53.7] vs. 70.5 [95% CI=65.5–75.8], respectively) and cumulative rates were similar between both groups (intervention, 106.2 [95% CI=100.2–112.5]; control, 101.5 [95% CI=95.6–107.8]). In the Compass trial, a transient increase in colposcopy referral rate was observed in the first round (cytology group, 2.7% [95% CI=1.8–3.9]; HPV + cytology group, 3.8% [95% CI=3.0–4.7]); HPV + dual-stain group, 3.9% [95% CI=3.1–4.9]) [8]. However, there was no significant difference in the total referral rate between the cytology and HPV groups after 12 months of follow-up. In addition, previous RCTs have suggested that hrHPV testing contributed to increased detection of CIN 3 compared with cytology alone in the first round [7,8]. We look forward to the follow-up results regarding the incidence of CIN3+ or worse as the primary endpoint of the study by Kono et al. [5].

Chiefly, the fundamental limitation of primary HPV screening is that effective screening has a marginal effect on the incidence of cervical cancer. A major barrier is the prevalence of ethnic, racial, and social disparities in incidence and mortality due to inequities in accessing screening tools [9]. Participation is also a barrier to effective screening, even in countries with organized screening programs. Self-sampling has been proposed as a means to increase accessibility and participation in screening services, reduce the workload of physicians, and lower the costs of screening. It may be an alternative for women who do not participate in screening programs [10].

In conclusion, primary HPV screening is effective in preventing cervical precancer and cancer. However, to eliminate cervical cancer, it is necessary not only to implement HPV screening programs but also to aim for high-coverage vaccination and concerted effort to increase participation in screening programs.

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