HPV testing for cervical cancer screening: Time for a new paradigm

Ronco G, Dillner J, Elfström KM, Tunesi S, Sjinjers P, Arbyn M, Kitchehner H, Segnan N, Gilham C, Giorgi-Rossi P, Berkhof J, Peto J, Meijer CJL; International HPV screening working group. (Center for Cancer Epidemiology and Prevention, AO City of Health and Science, Turin, Italy; Karolinska Institute, Stockholm, Sweden; VU University Medical Centre, Amsterdam, The Netherlands; Scientific Institute of Public Health, Brussels, Belgium; Institute of Cancer Sciences, University of Manchester, Manchester, UK; International Agency for Research on Cancer [IARC], Lyon, France; London School of Hygiene and Tropical Medicine, London, UK; Azienda Sanitaria Locale, Reggio Emilia, Italy.) Efficacy of HPV-based screening for prevention of invasive cervical cancer: Follow-up of four European randomised controlled trials. Lancet 2014;383:524–32.

SUMMARY

The present cluster analysis is a follow-up of four randomized trials that had previously compared human papillomavirus (HPV)-based screening with cytology-based screening. The authors now estimated the relative efficacy of these two methods among women who were being regularly screened, of the modifiers and the duration of protection. A total of 176,464 women aged 20–64 years were randomly assigned to HPV-based (experimental arm) or cytology-based (control arm) screening in Sweden (Swedescan), the Netherlands (POBASCAM), England (ARTISTIC) and Italy (NTCC) between 1997 and 2005. Women in the control arm had either liquid-based (ARTISTIC) or conventional (all other studies) cytological testing. Women in the experimental arm had either HPV testing alone, or both HPV testing and cytology. In ARTISTIC and NTCC, DNA testing of high-risk HPV types was done with the Hybrid Capture 2 assay using the 1 pg/μL (1 μg/L) recommended cut-off. PCR was done in POBASCAM and Swedescan.

The median follow-up was 6.5 years. Two rounds of screening were performed. The rate ratio for invasive cervical cancer in the experimental arm versus the control arm was calculated from enrolment to the end of observation and was found to be 0.56 (95% CI 0.40–0.89), with no heterogeneity between studies (p=0.52). Rate ratios were also calculated separately from the period of enrolment to 2.5 years and from 2.5 years to the end of the studies, and did not differ between the two arms for the first 2.5 years but was significantly lower in the experimental arm thereafter (0.45). Cumulative detection of invasive cervical carcinoma was similar in both arms up to about 2 years from enrolment, but diverged thereafter, reaching 46.7 per 100,000 (95% CI 32.1–65.5) in the experimental arm and 93.6 per 100,000 (95% CI 70.5–121.8) in the control arm 8 years after enrolment.

The rate ratio was also calculated for women who were HPV-negative at enrolment in the experimental arm and those who were cytology-negative at enrolment in the control arm and was found to be 0.50 (0.15–0.60). In screen-negative women, the cumulative incidence of invasive cervical cancer was also less in the HPV arm after 5.5 years (36.0 v. 8.7 per 100,000 women). The effect of women’s age on efficacy of HPV testing did not differ significantly between women aged 30–34 years and those who were ≥35 years (p=0.13).

Rate ratios were similar for various cancer stages, but were lower for adenocarcinoma (0.31, 95% CI 0.14–0.69) than for squamous cell carcinoma (0.78, 95% CI 0.49–1.25). Thus, HPV testing had a higher detection rate for adenocarcinoma. HPV-based screening provided 60%–70% greater protection against invasive cervical carcinoma as compared to cytology.

This study shows that earlier diagnosis of frankly invasive as well as microinvasive cervical cancer can be made by HPV testing and it should be used as a stand-alone test as co-testing leads to unnecessary colposcopy in many cases. It recommends screening with HPV every 5 years because recently acquired infections are mostly transient, with a potential for over-diagnosis.

COMMENT

Cervical cancer is the fourth most common cancer affecting women worldwide with approximately 528,000 new cases and 266,000 deaths every year.1 Almost 70% of the burden lies in areas with lower levels of development. It is most notable in the low-resource countries of sub-Saharan Africa and in many countries, about 7.9% among women with normal cytology, which makes a good case for using this as the method of primary screening. Only a small proportion of women who test positive will then need to be triaged for diagnosis of CIN, with the added assurance of accurate detection of at-risk women. The major drawback to HPV testing is that it is more expensive and requires laboratory infrastructure. A simple, affordable, accurate, point-of-care HPV test is awaited to facilitate screen-and-treat paradigms and minimize loss to follow-up. With these, it may be possible to screen women once or twice in a lifetime and eliminate the scourge of cervical cancer.
REFERENCES


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