Triaging a patient to colposcopy v. watchful waiting using current and prior HPV type and cytology result will help focus care on those at highest risk, and avoid overtreatment of women at low risk of cancer

sarah feldman[1]

[1]Brigham and Women's Hospital

April 3, 2022

Triaging a patient to colposcopy v. watchful waiting using current and prior HPV type and cytology result will help focus care on those at highest risk, and avoid overtreatment of women at low risk of cancer

Sarah Feldman MD MPH

Division of Gynecologic Oncology, Department of Obstetrics and Gynecology

Harvard Medical School

Brigham and Women's Hospital

75 Francis Street

Boston, Ma 02115

617-732-8840

sfeldman@bwh.harvard.edu

I have no conflicts of interest to disclose.

The findings by Gustafson, et al, that the rate of CIN2+ (high grade cervical precancers) was significantly higher in LLETZ specimens (32.4%) than in biopsies (14.7%) in Danish women age 45+ with type 3 transformations zone (ie part of the upper limit of the transformation zone is not visible) is based on a thoughtful analysis. Patients were screened and managed by Danish guidelines which included predominantly cytology based screening during the period of study, for all but women aged 60-64 (and some up to 69), with HPV testing only being offered to some women ages 30-59. Although the HPV test used in the study (Cobas) automatically provides HPV16 and 18 genotyping, this information was not used for triage. In this study all women underwent colposcopy and diagnostic LLETZ at the same visit. Although the Denmark guidelines recommend blind 4 quadrant biopsies for those without a visible lesion, endocervical curettage, which is a part of many other guidelines (Perkins RB, et al 2019 ASCCP risk-based management consensus guidelines for abnormal cervical cancer screening tests and cancer precursors. J Low Genit Tract Dis 2020;24:102–31), is not offered in Denmark. Although the diagnostic LLETZ picked up more CIN2+ than biopsy alone, as the authors state, the majority of women would not have needed the LLETZ if their risk could have been better predicted.

Can we use currently available technology and information to more effectively and safely triage patients to detect and treat high grade lesions but avoid aggressive and costly treatment for the majority? Many

studies have suggested that knowledge of a patients past screening history in addition to current results, in particular knowledge of the HPV status over time, whether HPV16 or 18 are present, as well as the severity of the cytology smear can help clarify who is at highest risk and who can be followed. (Egemen D, et al. Risk estimates supporting the 2019 ASCCP risk-based management consensus guidelines. J Low Genit Tract Dis 2020 Apr;24:132–43, Smith MA, et al. National experience in the first two years of primary human papillomavirus (HPV) cervical screening in an HPV vaccinated population in Australia: observational study. BMJ. 2022 Mar 30;376)

The underlying risk of the population studied affects the results and any downstream conclusions. In this case, the population studied had been predominantly screened by cytology, until the final screen, which was predominantly by HPV. Multiple studies have shown that HPV based screening has a better sensitivity than cytology alone and a reassuring result has as a more reliable negative predictive value than cytology, especially when lesions are in the endocervical canal or not fully visible. A prior negative or positive screen with an HPV based test might have aided in risk assessment and triage in this cohort. Adding p16ki67 staining to the initial cytology would also help to predict long term risk of high grade dysplasia, determining who could be followed and who treated. (Clarke MA, et al Five-Year Risk of Cervical Precancer Following p16/Ki-67 Dual-Stain Triage of HPV-Positive Women. JAMA Oncol. 2019 Feb 1;5(2):181-186.) Finally, an endocervical curettage, even with a brush, might have better sampled the endocervical canal and is less painful and costly than four blind biopsies.

Despite some of the limitations of the study, which the authors outline well, there is an important message- the CIN2+ rate in this older cohort of women is high- and if we are to prevent cervical cancer among older women, screening with HPV before exiting screening, and appropriately evaluating and treating women at risk of high grade dyspasia or cancer is essential.