Key Summary of Published Letter

Response to "Quality Improvement to Demonstrate the Lack of Reliability of the Human Papillomavirus mRNA Assay to Identify Women With Latent Human Papillomavirus Infections"

Background

- Investigators at Quest Diagnostics responded via published letter to an article by Cotton et al,[1] who recommended against the use of mRNA-based HPV testing as a first-line screening tool for cervical cancer.
- In the Cotton et al study,[1] investigators retrospectively examined the results of HPV mRNA tests performed November 2014 through June 2016 among women ≥30 who had at least 1 positive DNA-based HPV test result before November 2014.
- Among 425 women with a positive HPV DNA test and a subsequent mRNA test, 68.0% had negative results on the HPV mRNA test. Of these, 201 (69.6%) would have likely had their test followed up based on the negative mRNA result.
- The investigators concluded that mRNA-based HPV testing is not as sensitive as DNA-based HPV testing for detecting HPV infections.

Response

- In their response letter, Quest investigators pointed out limitations of the Cotton et al study.
  - A major limitation was that there was no clinical follow-up, meaning that clinical sensitivity and specificity could not be directly assessed.[1]
- The Quest investigators also cited other studies that contradicted Cotton et al's conclusions.
  - Two recent head-to-head comparisons and a review of over 60 studies showed that mRNA- and DNA-based HPV testing methods have comparable sensitivity for detecting high-risk lesions, with mRNA-based testing exhibiting superior specificity.[2-4]
- Further, the investigators provided data from their own experience.
  - They analyzed de-identified HPV test results of 34,640 women (30-65 years of age) in the United States who had follow-up colposcopy or biopsy within 6 months; 19,228 had mRNA-based HPV test results and 15,412 had DNA-based HPV test results.
  - Of the 34,640 women, 714 women had high-grade lesions (CIN3+), of whom 73 were determined to have cancer.
  - **Sensitivity results:** The mRNA- and DNA-based HPV testing methods did not significantly differ in sensitivity for detection of high-grade lesions (*P*=0.4).
    - mRNA-based HPV testing: 98.5%
    - DNA-based HPV testing: 97.1%
  - **Specificity results:** mRNA-based HPV testing was significantly more specific than DNA-based HPV testing for detection of high-grade lesions (*P*<0.001).
    - mRNA-based HPV testing: 19.4%
    - DNA-based HPV testing: 13.4%

Conclusions

- Based on the experience of Quest Diagnostics, as well as evidence from multiple studies,[2-4] the authors have responded that mRNA-based HPV testing is appropriate for use as a first-line screening tool for cervical cancer.

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Webpage

https://journals.lww.com/greenjournal/Citation/2018/09000/Quality_Improvement_to_Demonstrate_the_Lack_of.36.aspx

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