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No Risk for CVD, Ca With Vaginal Estrogen Use

— Findings were similar among those with or without hysterectomy

by Kristen Monaco, Staff Writer, MedPage Today

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PHILADELPHIA -- Vaginal estrogen use was found to be safe among postmenopausal women, researchers reported here.

In the prospective cohort study, Carolyn J. Crandall, MD, MS, of the University of California Los Angeles, and colleagues, found vaginal estrogen use was not associated with any increased risk for a global index event (GIE) (HR 0.69, 95% CI 0.59-0.81).

Presented at the annual meeting of [The North American Menopause Society](#), the findings were similar among users with an intact uterus (HR 0.63, 95% CI 0.51-0.77) or who have undergone a hysterectomy (HR 0.83, 95% CI 0.63-1.08) after adjustment for age, education, prior estrogen use, and a history of cancer, CVD, or DVP/PE.

Crandall explained to *MedPage Today* that her group wished to conduct this study because there was an absence of long-term data of a large cohort of those who used estrogen vaginally.

Based on results from the Women's Health Initiative, the [FDA requires warnings on all estrogen formulations](#).

She noted that "even the vaginal estrogens are required to have a black box warning that says 'caution, increased risk of stroke, breast cancer, possible dementia,' etc. And so currently, many leaders in the menopause field are wondering about whether that class labeling is unfair, essentially based on inadequate evidence, and they want to see whether that ought to be reconsidered."

The prospective cohort study with data from Women's Health Initiative Observational Study included 45,663 postmenopausal women age 50-79 from 40 centers. None of the participants used system estrogen therapy during the median 7.2 years of follow-up. Vaginal estrogen use was self-reported by the women and included use of a cream or suppository.

The risk of a GIE included time to initial occurrence of death from any cause, coronary heart disease, invasive breast cancer, stroke, pulmonary embolism, hip fracture, colorectal cancer, or endometrial cancer.

Crandall's group also found no increased risk among individual cancer risks factors among the entire cohort of users with or without a uterus:

- Breast cancer: HR 0.86, 95% CI 0.62-1.18
- Colorectal cancer: HR 0.72, 95% CI 0.41-1.25

Similar findings were also reported regarding cardiovascular risk:

- CHD: HR 0.44, 95% CI 0.29-0.69
- Stroke: HR 0.63, 95% CI 0.40-0.98
- PE/DVT: HR 0.59, 95% CI 0.33-1.05

Hip fracture risk was also not elevated among the entire cohort of users (HR 0.49, 95% CI 0.26-0.92).

The biggest take-home message from these findings is reassurance to clinicians regarding the lack of any increased associated risk for heart disease, stroke, of cancer among vaginal estrogen users versus non-users, Crandall highlighted, adding that she wasn't particularly surprised to see these results.

Despite the several strengths of the study, including the large cohort, long follow-up period, and strict control of the variables, the findings are limited to the observational study design.

"Are those women using vaginal estrogen healthier for whatever reason, and that's why they didn't have heart disease and stroke and breast cancer? Maybe because they're thinner, they exercise more, access to medical care -- we tried to control for everything, but we can't rule it out that there could be some systemic effect. I think that would probably be the one caveat of the study."

She also suggested that last remaining question to still be investigated is the possible risk of endometrial cancer with long-term vaginal estrogen use. "And it could be possible theoretically, because you're using it up right near the uterus. So that would be the remaining caveat that I think that what needs more investigation, is what happens with long-term use in terms of the uterine safety."

Crandall did not report any disclosures. The research was funded by the National Institutes of Health.

Reviewed by [F. Perry Wilson, MD, MSCE](#) Assistant Professor, Section of Nephrology, Yale School of Medicine and [Dorothy Caputo, MA, BSN, RN](#), Nurse Planner

Primary Source

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Source Reference: [Crandall C, et al "Breast cancer, endometrial cancer, and cardiovascular events in participants who used vaginal estrogen in the WHI observational study" NAMS 2017; Abstract S-1.](#)