

## **Estrogen Linked to Gallbladder Disease in Randomized Trial**

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Postmenopausal women who use conjugated equine estrogens (CEE) or estrogen plus progestin are at increased risk of biliary tract disease, according to findings from a randomized trial of healthy women. The elevated risks ranged from 54% to 93% depending on the estrogen and disease type.

"The association between estrogen therapy and gallbladder disease was suggested as early as 1975," senior author Dr. Robert B. Wallace, from the University of Iowa in Iowa City, told Reuters Health. "Since then, there have been a handful of observational studies that have supported or refuted the link," but just one randomized trial has looked at this topic, he added.

In the Heart and Estrogen/progestin Replacement Study (HERS), estrogen therapy was associated with an increased risk of biliary tract surgery. However, unlike the current randomized trial, which was limited to healthy women, HERS included women with known cardiovascular disease.

Using data from the Women's Health Initiative (WHI) trials, Dr. Wallace's team assessed the risk of gallbladder disease in postmenopausal women with or without hysterectomy. The former group included 8376 women who were randomized to receive CEE or placebo, whereas the latter included 14,203 women who were randomized to receive estrogen plus progestin or placebo.

The researchers' findings appear in the January 19th issue of the Journal of the American Medical Association.

In both groups of women, estrogen therapy was associated with a heightened risk of any gallbladder event. For example, among women with hysterectomy, 78 events per 10,000 person-years were noted in the CEE group compared with 47 events per 10,000 person-years in the placebo group.

Compared with controls, women treated with CEE or estrogen plus progestin were 80% and 54% more likely, respectively, to develop cholecystitis. In terms of cholelithiasis, the corresponding elevated risks were 86% and 68%.

Estrogen therapy raised the risk of cholecystectomy in both groups of women, but did not affect rates of other biliary tract surgery, the investigators found.

The link between estrogen therapy and gallbladder disease will probably not influence clinical decision-making to the extent that estrogen's association with heart disease and cancer has, Dr. Wallace said. Still, given the morbidity and costs, "the risk of gallbladder disease needs to be discussed when a doctor and patient are considering estrogen therapy."

*Cirillo DJ, Wallace RB, Rodabough RJ, et al. Effect of Estrogen Therapy on Gallbladder Disease. JAMA 2005;293:330-339.*