

Accelerated Accumulation of Multimorbidity After Bilateral Oophorectomy: A Population-Based Cohort Study

Walter A. Rocca, MD, MPH; Liliana Gazzuola-Rocca, MD; Carin Y. Smith, BS; Brandon R. Grossardt, MS; Stephanie S. Faubion, MD; Lynne T. Shuster, MD; James L. Kirkland, MD, PhD; Elizabeth A. Stewart, MD; and Virginia M. Miller, PhD

Abstract

Objective: To study the association between bilateral oophorectomy and the rate of accumulation of multimorbidity.

Patients and Methods: In this historical cohort study, the Rochester Epidemiology Project records-linkage system was used to identify all premenopausal women who underwent bilateral oophorectomy before age 50 years between January 1, 1988, and December 31, 2007, in Olmsted County, Minnesota. Each woman was randomly matched to a referent woman born in the same year (± 1 year) who had not undergone bilateral oophorectomy. We studied the rate of accumulation of 18 common chronic conditions over a median of approximately 14 years of follow-up.

Results: Although women who underwent bilateral oophorectomy already had a higher multimorbidity burden at the time of oophorectomy, they also experienced an increased risk of subsequent multimorbidity. After adjustments for 18 chronic conditions present at baseline, race/ethnicity, education, body mass index, smoking, age at baseline, and calendar year at baseline, women who underwent oophorectomy before age 46 years experienced an increased risk of depression, hyperlipidemia, cardiac arrhythmias, coronary artery disease, arthritis, asthma, chronic obstructive pulmonary disease, and osteoporosis. In addition, they experienced an accelerated rate of accumulation of the 18 chronic conditions considered together (hazard ratio, 1.22; 95% CI, 1.14-1.31; $P < .001$). Several of these associations were reduced in women who received estrogen therapy.

Conclusion: Bilateral oophorectomy is associated with a higher risk of multimorbidity, even after adjustment for conditions present at baseline and for several possible confounders. However, several of these associations were reduced in women who received estrogen therapy.

© 2016 Mayo Foundation for Medical Education and Research. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>) ■ Mayo Clin Proc. 2016;■(■):1-13

This study was prompted by 2 important areas of uncertainty: the risk and benefits of bilateral oophorectomy for the prevention of ovarian cancer and the role of sex hormones in regulating the aging process. Our group¹⁻³ and others⁴⁻⁶ have found that for most women without a cancer indication, the long-term risks of bilateral oophorectomy performed before menopause are greater than the benefits; therefore, the surgery should be limited to women who have a high-risk genetic variant predisposing to cancer.^{3,5} However, other authors continue to argue that, in the absence of a randomized clinical trial, the evidence against

prophylactic oophorectomy derived from observational studies is not sufficient to change the practice.⁷⁻¹⁰

Studies of the effects of sex steroids, in particular of estrogen, in regulating the aging process in humans have been hampered by the difficulty of measuring aging processes at the cellular, tissue, organ, or system level in vivo.¹¹ Ferrucci and his team from the Intramural Research Program at the National Institute on Aging have suggested using the accumulation of multimorbidity as a proxy measure for accelerated aging.¹²⁻¹⁶

Using 18 aging-related chronic conditions, we addressed 2 major questions: (1) whether



From the Division of Epidemiology (W.A.R., L.G.-R.), Department of Health Sciences Research (W.A.R.), Department of Neurology (W.A.R.), Women's Health Research Center (W.A.R., S.S.F., E.A.S., V.M.M.), Division of Biomedical Statistics and Informatics (C.Y.S., B.R.G.), Women's Health Clinic, Division of General Internal Medicine

Affiliations continued at the end of this article.

bilateral oophorectomy accelerates the accumulation of multimorbidity and (2) whether estrogen therapy (ET) modifies this accumulation.

PATIENTS AND METHODS

Bilateral Oophorectomy and Referent Cohorts

The Mayo Clinic Cohort Study of Oophorectomy and Aging-2 (MOA-2) is a recently established population-based cohort study, completely independent from our previous work on this topic.^{1,2} We included a cohort of women who underwent bilateral oophorectomy and a cohort of age-matched referent women representative of a geographically defined population. All data collection was through the records-linkage system of the Rochester Epidemiology Project (REP) that has been described extensively elsewhere.¹⁷⁻²⁰

We used the electronic index of the REP to identify women whose medical record included a code from the *International Classification of Diseases, Ninth Revision (ICD-9)* for either unilateral (65.3x and 65.4x) or bilateral (65.5x and 65.6x) oophorectomy between January 1, 1988, and December 31, 2007. We included women who underwent bilateral oophorectomy or a second unilateral oophorectomy before the onset of menopause and before reaching the age of 50 years, regardless of concurrent or prior hysterectomy. Although hysterectomy is a cause of surgical menopause, women with prior hysterectomy were included because hysterectomy was not considered a cause of ovarian insufficiency. However, we excluded women who underwent oophorectomy for ovarian cancer (primary or metastatic), to treat another estrogen-sensitive malignant disorder (usually breast cancer), or because they had high genetic risk of cancer (eg, carriers of *BRCA1* or *BRCA2* variants).

For each woman included in the bilateral oophorectomy cohort, we defined the date of the surgical procedure as the index date, and we selected via simple random sampling a woman from the Olmsted County population who was born in the same year (± 1 year) and had not undergone bilateral oophorectomy before the index date. All women who met these criteria were considered eligible regardless of menopausal status, any possible diseases or risk factors, and of prior hysterectomy or

unilateral oophorectomy. The complete medical records of the women with oophorectomy and the referent women underwent extensive manual abstraction by a physician (L.G.-R.) or a trained study nurse to confirm the oophorectomy status and to obtain clinical data. Thus, the final classification of women was based on the findings from medical record review. [Figure 1](#) presents detailed flowcharts for the 2 cohorts. All study procedures were approved by the institutional review boards of the Mayo Clinic and Olmsted Medical Center.

Baseline Conditions and Risk Factors

The complete medical records of women in both cohorts were manually abstracted for demographic, reproductive history, family history of cancer, and life habits information. In addition, the records were searched electronically for all *ICD-9* codes entered by any health care institution participating in the REP before the index date to identify conditions that were already present at baseline. These *ICD-9* codes were used to define the 20 chronic conditions recommended by the US Department of Health and Human Services (DHHS) to study multimorbidity.²¹⁻²⁴ However, we excluded from the DHHS list human immunodeficiency virus infections, autism spectrum disorders, and hepatitis because they were rare in our population and were not considered related to the aging process, and we added anxiety to the DHHS list because it was common in our population and was considered related to the aging process (18 selected conditions).²⁵ The condition labeled *schizophrenia* was retained because it included other psychoses that were common in the elderly population. To reduce the risk of false-positive diagnoses, only women whose medical record contained at least 2 diagnostic codes for a given condition separated by more than 30 days were considered to have that particular condition. For diagnostic codes entered before 1994, we required a 1-year separation because a finer dating of the codes in our system was impossible during that time frame.²³⁻²⁵

Outcome Conditions and Multimorbidity

For each woman, the diagnostic indices of the REP were also searched electronically for all *ICD-9* codes entered into the medical record by any health care institution participating in

Download English Version:

<https://daneshyari.com/en/article/8674077>

Download Persian Version:

<https://daneshyari.com/article/8674077>

[Daneshyari.com](https://daneshyari.com)