Benefits of Ovarian Conservation at the Time of Hysterectomy for Benign Disease

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Of the 600,000 hysterectomies performed yearly in the U.S., approximately 300,000 are accompanied by prophylactic bilateral oophorectomy, traditionally suggested as the best strategy to decrease the rate of ovarian cancer. However, excluding women from high-risk families, ovarian cancer is a relatively uncommon malignancy. At age 50, only about one in 1,500 women will be diagnosed with ovarian cancer and at age 70, the age of peak incidence, only 1 in 400 will be found to have ovarian cancer. In fact, while 16,000 women die of ovarian cancer every year, 70,000 die of lung cancer, 28,000 die of colon cancer and 40,000 die of breast cancer. Notably, 490,000 women die of heart disease every year and about 48,000 women die within one year following hip fracture.

Benefits of the Postmenopausal Ovary
Premenopausal oophorectomy causes an immediate loss of all ovarian hormones. Following menopause, the ovary continues to produce androstenedione and testosterone in significant amounts until age 80 and these androgens are converted in fat, muscle and skin into estrone. Following oophorectomy, menopausal women have significantly lower levels of androstenedione and testosterone than naturally menopausal women.

Oophorectomy has been shown to increase the risk of cardiovascular disease, the major cause of death for women. Oophorectomy after age 50 increases the risk of developing a first MI by 40% (RR 1.4, CI 1.0-2.0). Both estrogens and androgens inhibit bone resorption, and androgens increase bone formation. One study found that after 16 years of follow-up, women who were postmenopausal at the time of oophorectomy had 54% more osteoporotic fractures than women with intact ovaries. And, women older than 60 have a twofold increase in mortality (OR 2.18, CI 2.03-2.32) within a year following a hip fracture.

Our Study
The ideal way to study risks and benefits of oophorectomy would be with a prospective, randomized trial. However, that study would require 8,000 women to be randomized to oophorectomy or ovarian conservation and then followed for 40 years to ascertain causes of mortality. It is unlikely that this kind of study will ever be performed.

Therefore, in order to study the risks and benefits of prophylactic oophorectomy, we used a Markov computer model that can help to make complex medical decisions. We reviewed the literature for studies that examine the incidence of disease and mortality from 5 conditions that appear to be related to ovarian hormones: (CHD), ovarian cancer, breast cancer, stroke and hip fracture, as well as data for death from all other causes. We then found data for the relative risk of developing these five conditions for women having either oophorectomy or ovarian conservation between the ages of 40 and 75. Next, we calculated risk estimates for these conditions for every 5-year interval until women in our model either died or reached the age of 80. We deliberately chose to measure mortality because good data for quantifying morbidity or quality of life is not available.

Study Results
For women who have a hysterectomy with ovarian conservation at ages 50-54 and who are not at high risk of ovarian cancer, coronary , osteoporosis, breast cancer, or stroke, the probability of surviving to age 80 was 62.46%, compared to 53.88% if oophorectomy was performed. This 8.58% difference in survival is primarily due to fewer women dying of CHD and hip fracture, far outweighing
the 0.47% mortality rate from ovarian cancer. If surgery occurs at ages 55-59, the survival advantage is 3.92%, but after age 64 there was no significant difference in survival. (see graph)

For a hypothetical group of 4,000 women ages 50 to 54 undergoing hysterectomy with oophorectomy, our analysis predicts 343 excess deaths (mostly from CHD). For the risk of ovarian cancer to outweigh the risks of CHD and hip fracture following oophorectomy, CHD deaths would need to be 95% lower than what the rates among women are currently.

Although quality of life issues are of great importance to women, data were not available to include these in our model. Premenopausal, and for some post-menopausal women, oophorectomy may lead to the onset of hot flushes and mood disturbances, a decline in a sense of well-being, a decline in cognitive functioning, poor sleep quality, depression and a decline in sexual desire and frequency. While estrogen therapy may reduce both these symptoms, only 17% of women have continued hormone therapy after the WHI and fewer now start hormones at the time of menopause. Also, the number of patients still taking either statins or Bisphosphanates after 1 year is less than 20%. Therefore, any assumption that can decrease risks following oophorectomy is questionable.

The results of our model suggest that the decision to perform prophylactic oophorectomy should be approached with great caution for the majority of women who are at average risk of developing ovarian cancer and who are under the age of 65. The American College of Obstetricians and Gynecologists recommends that “the decision to perform prophylactic oophorectomy should be based not only on the patient's age but also on other factors that weigh individual risk for developing ovarian cancer against loss of ovarian function”. Hopefully, our results will encourage a dialogue between and women who are considering ovarian conservation or oophorectomy.

Abstract

Ovarian Conservation at the Time of Hysterectomy for Benign Disease

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Objective: Prophylactic oophorectomy is often recommended concurrent with hysterectomy for benign disease. The optimal age for this recommendation in women not at high risk for ovarian cancer has not been determined.

Methods: Using published age-specific data for absolute and relative risk, both with and without oophorectomy, for ovarian cancer, coronary heart disease (CHD), hip fracture, breast cancer, and stroke, a Markov decision analysis model was used to determine the optimal strategy to maximize survival for women not at high risk of ovarian cancer. For each 5-year age group from 40-80, four strategies were compared: ovarian conservation or oophorectomy; and use of ERT or non-use. Outcomes as proportion of women alive at age 80 were measured. Sensitivity analyses were performed varying both relative and absolute risk estimates across the range of reported values.

Results: Ovarian conservation until age 65 benefits long-term survival for women undergoing hysterectomy for benign disease; women with oophorectomy before age 55 have 8.38% excess mortality by age 80 and before age 59 have 3.92% excess mortality. There is sustained, but decreasing, benefit until the age of 75, when excess mortality for oophorectomy is less than 1%. These results were unchanged following multiple sensitivity analyses and were most sensitive to the risk of coronary heart disease.

Conclusion: Ovarian conservation until at least age 65 benefits long-term survival for women not at high risk of ovarian cancer when undergoing hysterectomy for benign disease.

References:

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