

Adiposity Magnifies Oophorectomy's CV Impact

Finding may change practice for preventing breast, ovarian cancer in BRCA1 and -2 mutation carriers.

BY BRUCE JANCIN

FROM THE SAN ANTONIO BREAST
CANCER SYMPOSIUM

SAN ANTONIO – Prophylactic bilateral oophorectomy is the standard of care for prevention of breast and ovarian cancer in BRCA1 and -2 mutation carriers, but the benefit may be outweighed by sharply increased subsequent all-cause mortality, mostly due to cardiovascular disease, when oophorectomy is performed in obese women at a young age, a study has shown.

“This could have very clear relevance for clinical practice. Those women who’ve had oophorectomy in the past may need to be followed more carefully and encouraged to maintain a healthy weight.

“And these findings may also play into planning about prophylactic surgery, as well – weighing a woman’s cardiovascular risk and obesity level in deciding whether to do a prophylactic oophorectomy,” Dr. Anne Marie McCarthy said at the symposium.

Prophylactic oophorectomy as a strategy for prevention of ovarian and breast cancer in BRCA mutation carriers is too recent a development for follow-up studies to be sufficiently mature to assess the cardiovascular impact of abrupt surgical deprivation of estrogen and androgens in premenopausal women. After all, the longest follow-up reported to date in such studies is only 6 years.

For this reason, Dr. McCarthy and her coworkers turned instead to the third National Health and Nutrition Examination Survey (NHANES III), where they zeroed in on a nationally representative sample of women aged 40 or older when interviewed during 1988-1994. They compared 474 women who had previously undergone bilateral oophorectomy, with 3,047 women with intact ovaries. Through 2006, 1,106 women had died.

Women with bilateral oophorectomy were typically older, more likely to be of lower socioeconomic and educational status, and had higher usage of hormone therapy than did those with intact ovaries.

In a multivariate analysis adjusted for these and other potential confounding factors, women with a body mass index of 30 kg/m² or more who underwent oophorectomy before age 40 had a 2.4-fold greater risk of all-cause mortality than women with intact ovaries ($P = .004$).

The risk was similarly increased in users and never-users of hormone therapy, according to Dr. McCarthy of Johns Hopkins University, Baltimore.

Obesity was also independently associated with increased all-cause mortality in the overall study population, where a BMI of 30 kg/m² or more conferred a 37% greater risk than seen in women with a BMI of less than 25 kg/m² ($P = .001$).

However, this adiposity-related increase in mortality risk was further magnified nearly sevenfold when obese women who underwent oophorectomy prior to age 40 were compared with obese women with intact ovaries.

Session cochair Dr. Graham Colditz said the new NHANES III analysis is consistent with an earlier report from the Nurses’ Health Study (Obstet. Gynecol. 2009;113:1027-37), which showed increased mortality from coronary heart disease and stroke in participants who underwent bilateral oophorectomy. Moreover, this risk was increased most dramatically in nurses with oophorectomy at a young age.

But there is an important and potentially worrisome difference between the Nurses’ Health Study population and women who undergo prophylactic bilateral oophorectomy today, he added. Enrollment in the Nurses’ Health Study began in the mid-1970s, and 70% of participants had a BMI below 25 kg/m².

“Many of us can barely remember the days when the majority of U.S. women had a BMI less than 25 kg/m²; we’ve now shifted to where 70% are over 25 kg/m²,” noted Dr. Colditz, professor of surgery at Washington University in St. Louis.

If the new NHANES III analysis is indeed correct and adiposity accentuates the adverse cardiovascular impact of bilateral oophorectomy performed at a young age, then the ongoing obesity epidemic spells trouble for the strategy of prophylactic oophorectomy for the prevention of breast and ovarian cancer.

“Are women really thinking about

their overall mortality risk when they decide about prophylactic oophorectomy, or are they focusing on breast cancer mortality and disease-free survival?” he asked.

Dr. Carol J. Fabian commented that Dr. McCarthy’s study dovetails nicely with an earlier Mayo Clinic report (Lancet Oncol. 2006;7:821-8) showing that women who underwent oophorectomy before age 45 not only had a dramatic increase in cardiovascular mortality, they also had increased rates of Parkinson’s disease and self-reported cognitive deficits.

The good news: All of these increased risks were negated by hormone therapy with estrogen alone, which was an option because many of these women underwent hysterectomy at the time of oophorectomy, she said.

“It’s a really important point: If we’re going to perform oophorectomy on these very high-risk women at a very young age, there are going to be more cardiovascular outcomes, and we have to really think hard about how to prevent these,” noted Dr. Fabian of the University of Kansas Cancer Center in Kansas City.

The NHANES III analysis is particularly relevant because prophylactic oophorectomy is generally recommended in BRCA mutation carriers after their last child is born or after age 35, but before age 45, whichever comes first.

“These women are getting oophorectomy at an extremely young age,” she noted.

Dr. McCarthy said she had no relevant financial disclosures. ■

Patients’ Knowledge Gaps May Hamper Breast Ca Follow-Up

BY SUSAN LONDON

FROM THE ANNUAL MEETING OF THE NORTH
AMERICAN PRIMARY CARE RESEARCH GROUP

SEATTLE – Many women who have had early breast cancer don’t know key treatment facts that may have implications for their long-term follow-up and health, according to a survey of cancer survivors.

Among nearly 500 respondents who had completed

efficacy in navigating survivorship care, most of the women believed that they could clearly communicate their treatments to health care providers outside their oncology clinic, reported Dr. Jun James Mao.

“We need to begin designing interventions to allow the accurate transfer of cancer treatment information, as well as to promote self-efficacy among a diverse group – especially among individuals who are particularly vulnerable to health disparities, such as racial/ethnic minorities and elderly patients,” noted Dr. Mao, director of integrative medicine at the Hospital of the University of Pennsylvania, Philadelphia.

The investigators surveyed women from the university’s outpatient breast cancer oncology clinic who were participating in a study of aromatase inhibitors. All had stage 0-III breast cancer, had completed primary treatment, and were taking one of those agents. The women were classified as knowing a given aspect of their cancer or treatment if their response on the questionnaire matched the information in their chart.

They were classified as not knowing if they answered that they did not know or if their response did not match the chart information.

The mean age of the 490 participating women was 62 years. In all, 82% of participants were white, 14.5% were black, 1.8% were Asian, 1% were Hispanic, and the rest were of other races/ethnicities. The majority had a college education (43%) or graduate/professional education

(36%). About a third each had received their diagnosis less than 2 years, 2-5 years, and more than 5 years in the past.

Study results showed that substantial proportions of women did not know their breast cancer stage (49%), ER status (26%), progesterone receptor status (75%), HER2 status (58%), whether they had had lymph nodes removed (16%), and whether they had any positive lymph nodes (15%). Only 5% did not know if they had received chemotherapy. Among the group of patients who underwent chemotherapy, nearly half (44%) did not know all of the agents they had received, although the value was somewhat lower (21%-29%) for individual agents. That finding is “strongly troubling,” Dr. Mao said, given that “chemotherapy is one of the greatest sources of long-term late effects.”

Of particular note, despite the gaps seen in knowledge about treatment, 88% of the women agreed or strongly agreed that “I can communicate clearly about my cancer treatment(s) to other health care providers.”

“One of the most striking differences we found was the racial/ethnic difference in cancer knowledge and self-efficacy,” Dr. Mao noted. In multivariate analyses, relative to their white counterparts, women who were not white had significantly lower scores for knowledge (14.5 points lower) and self-efficacy (13.5 points lower).

In addition, women had lower levels of knowledge if they were older, had less education, received chemotherapy, or were a longer time out from diagnosis. And they had lower levels of self-efficacy if they were older and less educated. ■

VITALS

Major Finding: Many women did not know their cancer’s ER status (26%), whether they had had lymph nodes removed (16%), and all of the chemotherapy drugs they had received (44%). But most (88%) nonetheless believed they could clearly communicate their treatments to health care providers.

Data Source: A cross-sectional survey of 490 women who had completed primary treatment for stage 0-III breast cancer.

Disclosures: Dr. Mao reported that he had no relevant financial disclosures.

primary treatment, one in four didn’t know their cancer’s estrogen receptor (ER) status, and one in six didn’t know whether they had had any lymph nodes removed. In addition, nearly half of those who had undergone chemotherapy were unable to correctly identify all of the agents they had received, according to survey results.

Yet when asked questions about their perceived self-