

SABCS: Low-Fat Diet Helps Prevent Breast Cancer Relapse

SAN ANTONIO, Dec. 16 -- A diet with 20% of calories from fat, or less, may help reduce risk of breast cancer recurrence, particularly for women with hormone-receptor-negative disease, according to a large trial.

Among more than 2,400 women with early breast cancer followed for 5.8 years, there were 22% fewer deaths for those on the low-fat diet, although this difference was not significant, said Rowan T. Chlebowski, M.D., Ph.D., of Harbor-UCLA Medical Center in Torrance, Calif. But it was significant for a subset with estrogen-receptor-negative disease.

The randomized, prospective trial comparing a low-fat diet with a normal diet was presented at the San Antonio Breast Cancer Symposium and published simultaneously in the *Journal of the National Cancer Institute*.

The researchers reported a borderline significant improvement in relapse-free survival (hazard ratio 0.78, 95% confidence interval 0.60 to 0.98) and a nonsignificant benefit in overall survival (HR 0.89, 95% CI 0.65 to 1.21).

However, for the 362 women with estrogen- and progesterone-receptor-negative breast cancer, there was a 66% reduction in mortality for an 11% absolute survival advantage in the diet group (HR 0.47, 95% CI 0.29 to 0.78, $P=0.001$).

This benefit for hormone receptor negative cancers is as great as has been seen with any other treatment for this notoriously difficult to treat cancer type, said session moderator Richard Elledge, M.D., of Baylor College in Houston.

"This is a seminal study," he said. "They have fewer treatment options."

The National Cancer Institute-sponsored study randomized 975 women to a dietary intervention with the goal of reducing dietary fat to 15% of total calories. They attended eight biweekly, one-hour counseling sessions to learn about the low-fat eating plan, kept written records of their daily fat gram intake, met with or talked to dietitians every three months, and could attend optional monthly group sessions. The 1,462 women in the control group met with a dietitian when they started the trial and

were called by dietitians every three months.

All patients (mean age about 58) had early-stage breast cancer for which they underwent surgery and systemic therapy (tamoxifen for estrogen-receptor positive and chemotherapy for estrogen-receptor negative tumors). Radiation therapy was optional as was chemotherapy for estrogen-receptor-positive disease.

Though both groups started with a daily fat intake of about 56 to 57 grams (about 30% of total calories), the diet group dropped to an average of 33 grams per day (20.3% of total calories) while the control group stayed at 51 g/day (29.2% of total calories) at one year, which was sustained through the trial.

As might be expected, women in the intervention group lost an average of 1.1 kg/m² in body mass index and an average of 6.0 pounds more than those in the control group over five years (both $P < 0.005$).

At the 5.8-year point, the researchers reported (diet versus control):

0.4% and 0.8% had a local or regional recurrence,

5.5% and 6.6% had a distant recurrence,

3.2% and 3.8% had a second cancer, and

7.7% and 10.2% had a death from any cause.

In the subgroup analyses, the investigators reported:

Relapse free survival was not significantly different between intervention and control groups for the estrogen- and progesterone-positive women (HR 0.92, 95% CI 0.71 to 1.19),

Relapse-free survival was significantly improved for the women with hormone-receptor-negative breast cancer (HR 0.46, 95% CI 0.26 to 0.80),

Overall survival was not different between groups for women with hormone-receptor-positive cancer (HR 0.88, 95% CI 0.61 to 1.28, $P = 0.59$), and

Overall survival was significantly improved for women with hormone-receptor-negative breast cancer in

the dietary intervention (HR 0.34, 95% CI 0.16 to 0.70, $P=0.003$).

In an accompanying editorial, Victor Kipnis, Ph.D., of the National Cancer Institute, and colleagues, cautioned that while "this result may be of clinical relevance and suggests a possible adjuvant therapy for hormone-receptor-negative breast cancer patients," it was an unplanned analysis and needs confirmation.

Dr. Chlebowski agreed. "It's premature to say the benefit is all in receptor negative and receptor positive won't benefit," he said.

Dr. Kipnis and colleagues also warned oncologists that the effects of weight loss and dietary fat reduction are difficult to disentangle.

"The relation between dietary fat and breast cancer incidence and survival remains one of the most controversial hypotheses in nutritional epidemiology, with mostly observational studies showing rather inconsistent results," they added.

The study authors acknowledged that findings could have been confounded by the higher frequency of mastectomy in the diet group compared to the control group, but said adjusting for this did not eliminate the diet's advantage. Also, the study's funding ended before the full three years of planned post-intervention follow-up, which may have impacted data recovery, they said.

The researchers concluded that dietary fat reduction may be appropriate for some highly motivated women, but that the diet may be difficult for women to sustain without the assistance of a dietician or other support.

Dr. Elledge pointed out that there is little reason not to recommend such a diet for women who ask what else they can do to prevent breast cancer relapse. "It's good for other diseases as well," he said.

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