

Axillary Lymph Node Dissection: No Clear Benefit

BY MARY ANN MOON

FROM JAMA

Axillary lymph node dissection did not improve overall survival or disease-free survival in women with T1-T2 breast cancer who were found to have limited metastasis on sentinel node dissection.

In the American College of Surgeons Oncology Group's Z0011 trial, survival was nearly identical between women who underwent lumpectomy and sentinel node dissection alone, followed by adjuvant chemotherapy and tangential-field whole-breast irradiation, and women who underwent axillary node dissection when sentinel node biopsy revealed limited metastasis, followed by the same chemotherapy and irradiation.

"The findings from Z0011 document the high rate of locoregional control achieved with modern multimodal therapy, even without axillary lymph node dissection," said Dr. Armando E. Giuliano of John Wayne Cancer Institute at Saint John's Health Center, Santa Monica, Calif., and his associates.

The results also imply that axillary node dissection is no longer warranted in such patients, because "the only additional information gained ... is the number of nodes containing metastases. This prognostic information is unlikely to change systemic therapy decisions and is obtained at the cost of a significant increase in morbidity," the investigators noted.

Forgoing the standard practice of axillary node dissection when sentinel nodes reveal metastasis constitutes a practice change that "would improve clinical outcomes in thousands of women each year by reducing the complications associated with axillary lymph node dissection and improving quality of life with no diminution in survival," they concluded.

VITALS **Major Finding:** Overall 5-year survival was 91.8% with axillary node dissection and 92.5% without it; the 5-year disease-free survival was 82.2% with axillary node dissection and 83.9% without it. The differences were not significant.

Data Source: A phase III noninferiority trial involving 891 women with invasive node-positive breast cancer treated at 115 medical centers.

Disclosures: This study was supported by the National Cancer Institute. No financial conflicts of interest were reported.

The need for axillary node dissection when sentinel nodes are found to have metastasis has been called into question for years, and use of this "standard" practice has declined. Until now, "no study has conclusively demonstrated a survival benefit or detriment for omitting axillary node dissection," they said.

The ACS Oncology Group's Z0011 trial, begun in the late 1990s, was intended to definitively answer that question. The phase III "noninferiority" trial involved 891 women who were followed at 115 centers after undergoing lumpectomy and sentinel node dissection revealing metastasis. These subjects were randomly assigned to undergo standard axillary node dissection (445 patients) or no axillary node dissection (446 patients), followed by whole-breast tangential-field radiation (not third-field nodal irradiation) and whatever adjuvant systemic therapy their treating physicians deemed necessary.

The trial's enrollment was halted early in 2004 "because of concerns regarding the extremely low mortality rate." It was determined that accrual of more patients would not alter the survival findings, and final follow-up for the analysis was completed in 2010.

After a median of 6 years of follow-up, there were 94 deaths. The 5-year overall survival was 92.5% with sentinel node dissection alone and 91.8% with full axillary node dissection, a nonsignificant difference. The 5-year disease-free survival

rate was 83.9% with sentinel node dissection alone and 82.2% with full axillary node dissection, also a nonsignificant difference. These results were consistent across several subgroups of patients, regardless of patient age, tumor size, tumor hormone-receptor status, or which adjuvant therapies were received.

The two study groups did differ significantly in morbidities related to lymph node dissection. The rate of wound infection, axillary seromas, and paresthesias was markedly higher for women who

underwent axillary node dissection (70%) than for those who did not (25%). Lymphedema also was more common with axillary node dissection.

"The excellent local and distant outcomes in this study highlight the effects of multiple changes in breast cancer management" in recent years, including "improved imaging, more detailed pathological evaluation, improved planning of surgical and radiation approaches, and more effective systemic therapy," Dr. Giuliano and his colleagues said (JAMA 2011;305:569-75). They emphasized that this trial did not include patients who had mastectomy, lumpectomy without radiation therapy, partial-breast irradiation, or whole-breast irradiation in the prone position (which would not treat the low axilla). In such patients, "axillary lymph node dissection remains standard practice when sentinel lymph node dissection identifies a positive sentinel lymph node." ■

A Definitive Answer

The American College of Surgeons Oncology Group Z0011 trial "definitively showed that axillary lymph node dissection is not beneficial," said Dr. Grant Walter Carlson and Dr. William C. Wood.

Even though 27% of the women who underwent axillary node biopsy were found to have additional lymph nodes containing metastases, the axillary recurrence rates were similar between the two groups.

"Survival was independent of lymph node status and was so good in both groups that longer follow-up has little likelihood of demonstrating any difference between the [two] groups," they noted. "Taken together,

findings from these [and other] investigators provide strong evidence that patients undergoing partial mastectomy, whole-breast irradiation, and systemic therapy for early breast cancer with microscopic sentinel lymph node metastasis can be treated effectively and safely without axillary node dissection."

DR. CARLSON and DR. WOOD are at Winship Cancer Institute, Emory University, Atlanta. They reported no financial conflicts of interest. These comments were taken from their editorial that accompanied Dr. Giuliano's report (JAMA 2011;305:606-7).

VIEW ON THE NEWS

Oophorectomy Halves Risk of Some Contralateral Breast Ca

BY KERRI WACHTER

FROM A BREAST CANCER SYMPOSIUM SPONSORED BY THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY

NATIONAL HARBOR, MD. – Oophorectomy cut the risk of contralateral breast cancer by almost half in women with a family history of BRCA mutations, according to results of a retrospective study of more than 800 women. The benefit was even greater in women diagnosed with breast cancer before age 50.

"Oophorectomy was the most significant predictor of the development of contralateral breast cancer in this group of women," investigator Kelly A. Metcalfe, Ph.D., said.

Removing ovaries reduced the risk of contralateral breast cancer by 47% in the entire cohort (relative risk 0.53, $P = .007$), she reported. Women younger than age 50 had a 55% reduction (RR 0.45, $P = .002$), but oophorectomy had no effect on risk of contralateral breast cancer in women 50 and older.

The multicenter cohort study followed women from the date of breast cancer diagnosis until contralateral breast cancer was diagnosed, contralateral mastectomy was performed, death, or date of last follow-up.

Women were included if they were part of a family

with known BRCA1 or BRCA2 mutations, had stage I or II breast cancer, were 65 years or younger at the time of diagnosis, were diagnosed in 1975 or later, and had no previous cancer diagnosis. Investigators included living and deceased patients to avoid survivorship bias.

All told, 60% of the women had records of oophorectomy. The researchers reviewed 1,866 cases of breast cancer in 615 families. A total of 846 patients – 79% living – were eligible, gave consent, and had medical charts available for review.

The mean year of birth was 1950, and the mean age at diagnosis was 42 years. The women were followed for an average of 11.5 years. Nearly two-thirds (62%) had BRCA1 mutations, and 88% had undergone genetic testing. Among 177 women who died, breast cancer was the cause of death for 83%.

In the full study cohort, 18% were diagnosed with contralateral breast cancer with a mean time between the two diagnoses of 5.7 years. At 5 years, all women in the cohort had a 13% risk of developing contralateral disease, which rose to 34% at 15 years.

"Age was a very important predictor for these women. Women who were diagnosed with young-onset breast cancer (under the age of 50) had a significantly higher risk of developing contralateral breast

cancer within the first 15 years," said Dr. Metcalfe of the nursing faculty at the University of Toronto. For younger women, the risk was 38% at 15 years, compared with 18% in women 50 and older.

At 15 years post diagnosis, a woman younger than 50 years who had not had an oophorectomy had a roughly 60% risk of developing contralateral breast cancer. The risk was roughly 20% in women 50 years or older with intact ovaries.

Family history also appeared to play an important role.

Among the whole cohort, the risk of contralateral breast cancer increased by a third with every first-degree relative diagnosed with breast cancer under age 50. "This was particularly evident in BRCA1 carriers and early-onset breast cancer," said Dr. Metcalfe. Risk was increased by roughly 40% in each of these groups.

For women younger than 50 years at diagnosis who still have intact ovaries, the risk of developing contralateral breast cancer at 15 years was 58%. With the addition of two or more first-degree relatives diagnosed with breast cancer under the age 50, the 15-year risk rose to 68%.

The authors reported that they have no relevant financial relationships. ■