Local Therapy Benefits Stage IV Breast Cancer

BY PATRICE WENDLING
Chicago Bureau

ATLANTA — Contrary to conventional belief, results of a new study suggest that surgical removal of the primary tumor can benefit women with stage IV breast cancer.

Although overall survival was unchanged at 5 years, there was a better progression-free survival for women who underwent local therapy of the primary tumor when initially presenting with metastatic disease, Roshni S. Rao, M.D., reported at a symposium sponsored by the Society of Surgical Oncology.

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"This is important, because any time you can slow down the progression of the disease, it potentially gives other therapies a better chance at working," Dr. Rao told this newspaper. "It's entirely possible that as medical therapy improves, the metastatic progression-free survival seen in these patients will translate into a survival benefit."

The study joins a growing body of evidence that challenges traditional beliefs by suggesting that aggressive local therapy may prolong survival, said Dr. Rao, a breast-surgery fellow at the University of Texas M.D. Anderson Cancer Center, Houston.

Current treatment is generally directed at the sites of metastases, and the primary tumor is left intact. Surgery is undertaken only for palliation.

Only 3%-6% of American women diagnosed with breast cancer will be stage IV at presentation, but a staggering 50% of women internationally will present with metastatic disease, Dr. Rao said.

The retrospective, single-institution chart analysis included 224 women with stage IV breast cancer, including 142 patients who received systemic treatment without surgery and 82 who had surgery to remove the primary tumor and systemic therapy.

Of the surgical patients, 43 underwent mastectomies, and 39 had segmental resection.

All of the patients received hormonal therapy or chemotherapy within 3 months of diagnosis.

Both groups were similar in race, family and personal history of cancer, histology, tumor size, and estrogen- or progesterone-receptor status.

The surgical group was slightly younger than the nonsurgical group (49 years vs. 54 years); had one metastatic site (generally the liver); was more likely to receive chemotherapy than hormonal therapy as a first-line treatment; had a lower nodal stage (59 N0/N1 patients vs. 100); and was more likely to be Her2/neu positive (24 vs. 28 patients).

Initially, surgical patients demonstrated better survival than women who received systemic therapy alone. But this was not significant on final analysis, Dr. Rao said.

At 3 years, 119 of the 142 women (84%) in the nonsurgical group were alive, compared with 78 of the 82 women (95%) in the surgical group.

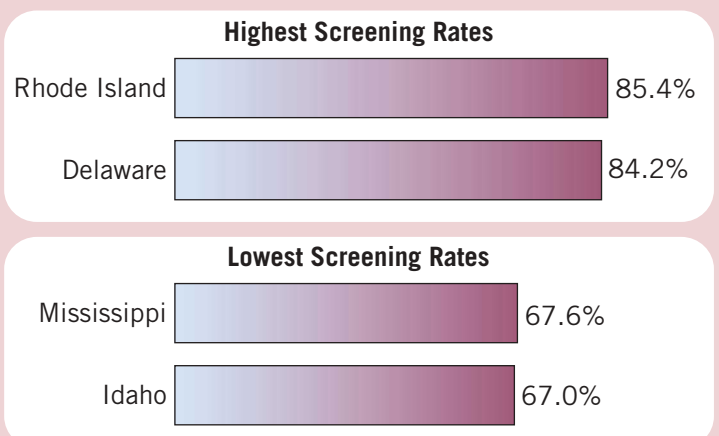
At final follow-up, there were 27 deaths in the nonsurgical group and 11 in the surgical group. Eleven patients who had surgical intervention at their primary site as well as their metastatic site had no evidence of disease during follow-up.

The only independent predictors of overall survival were having a single metastatic site and Her2/neu–negative status (hazard ratio 2.43 and 2.52, respectively).

Surgery and estrogen-negative status were the only independent predictors of metastatic progression-free survival (hazard ratio 0.47 and 0.6, respectively). ■

DATA WATCH

Patients Who Had a Mammogram During Preceding 2 Years



Note: Based on estimated data for patients aged ≥40 years from the Behavioral Risk Factor Surveillance System, 2002.
Source: Centers for Disease Control and Prevention

KEVIN FOLEY, RESEARCH/JULIE KELLER, DESIGN

Multiple Skin Leiomyomas May Portend Symptomatic Fibroids

BY BETSY BATES
Los Angeles Bureau

FLORENCE, ITALY — Multiple skin leiomyomas may be the first sign of multiple cutaneous and uterine leiomyomatosis, a hereditary disease that can include highly symptomatic uterine fibroids and, in a small percentage of cases, aggressive renal cancer, N. Afrina Alam, M.B., reported at the 13th Congress of the European Academy of Dermatology and Venereology.

If uterine leiomyomas develop as part of the syndrome, they tend to be 'very severely symptomatic with a high risk of hysterectomy.'

Dr. Alam has been working with a multidisciplinary team studying this disease, once thought rare. Just 20 cases had been reported worldwide a few years ago when she began studying multiple cutaneous and uterine leiomyomatosis (MCUL), said Dr. Alam, formerly of the Centre for Cutaneous Research at St. Bartholomew's Hospital and the London.

Cutaneous leiomyomas appear in patients in their teens or 20s, and they are "very variable in their severity," said Dr. Alam, now of St. John's Institute of Dermatology at St. Thomas Hospital in London. She found 50 index cases herself, and in the ensuing years, significantly more cases have been identified in the United Kingdom and elsewhere.

In a study of 108 patients with MCUL, the mean number of skin leiomyomas was 25. Nearly 90% of patients reported at least one painful skin lesion.

Skin lesions tend to predate other manifestations of the disease by 5-10 years, making them critically important in terms of their diagnostic relevance, Dr. Alam said.

If uterine leiomyomas develop as part of the syndrome, they are histologically indistinguishable from other fibroids but tend to be "very severely symptomatic, with a high risk of hysterectomy," she said. By age 55, more than half of women with the syndrome had undergone hysterectomies.

The UK team identified aggressive renal cancer in 9 of 89 families carrying the multiple leiomyomatosis gene. One study subject died of metastatic renal carcinoma at age 18 years.

Researchers who have studied the MCUL's genetic profile have found that highly penetrant mutations in an enzyme on chromosome 1 cause the condition, an autosomal dominant disease. A host of mutations has been found in affected families, and certain patterns have emerged.

For example, a mutation dubbed G354R FH appears to be associated with uterine fibroids without skin manifestations. Certain truncating mutations, especially frameshift mutations, appear to be linked to development of renal cancer, which was far more common in females than in males in the MCUL study.

Among 26 males carrying any MCUL mutation, all 26 had skin leiomyomas. Among 67 female mutation carriers, 46 had both skin and uterine leiomyomas, 10 had only skin leiomyomas, and 5 had only uterine leiomyomas. Mutations in six patients were nonpenetrant. ■

Better Counseling Facilitates Decision Making After Testing

NEW YORK — Enhanced counseling can help women at high risk of breast or ovarian cancer make better use of the information they receive from genetic testing for *BRCA1* and *BRCA2* mutations, according to a study presented in poster form at a cancer symposium sponsored by New York University.

The few studies that have examined the effects of genetic testing on decision making have found that a significant proportion of eligible women don't take any action after learning their genetic status, according to Suzanne Miller, Ph.D., of Fox Chase Cancer Center in Philadelphia, and her associates.

The investigators randomized approximately half of the study's 80 women who were at high risk for ovarian cancer based on family history to receive "enhanced counseling" before genetic testing.

This process was aimed at helping the women "prelive" how they might respond to their test results.

"We wanted to help women anticipate how they would react, so they would be prepared for it," Dr. Miller, the study's lead investigator, said during an interview.

Six months later, 68% of the women in the intervention group had sought prophylactic oophorectomy information, and 28% had undergone the surgery. In the control group, which had received standard counseling along with information about improving their general health, 26% had sought information on oophorectomy and 6% had had the surgery.

"The women in the intervention arm were in a position to take action when they got their results," Dr. Miller said. "This indicates that enhanced counseling can play an important role in decision-making after *BRCA1* and *2* testing."

The symposium was also sponsored by the Lynne Cohen Foundation for Ovarian Cancer Research.

—Gina Shaw