Women with High Risk Locally Advanced Cancers can be Safely Treated with Lumpectomy

Abstract: Biology, Not choice of Mastectomy versus Lumpectomy, Dictates Recurrence in High-Risk Breast Cancer

May 4, 2012, Phoenix--Women with high-risk tumors can be safely treated with lumpectomy if their tumors respond well to chemotherapy prior to surgery (neoadjuvant chemotherapy), suggests a new study presented this week at the American Society of Breast Surgeons (ASBrS) Annual Meeting. The study examined cancer recurrence in areas near the original tumor site (local recurrence) in high-risk women who received multidisciplinary cancer therapies. It found that tumor biological characteristics, reflected in part by response to neoadjuvant chemotherapy, and not choice of mastectomy or breast conserving lumpectomy was the major determinant of cancer returning locally.

“Traditionally, the choice of surgical treatment was thought to have the greatest impact on local recurrence, especially in women with significant tumor remaining after pre-surgical chemotherapy,” explains Dr. Elizabeth Cureton, Breast Surgical Oncology Fellow, University of California, San Francisco Medical Center. “But this was not the case. In fact, the study found that tumor characteristics such as gene expression, advanced stage, and the poor response to neoadjuvant therapy itself were the major predictors of cancer recurrence.”

The study, part of the I-SPY 1 trial, examined 206 patients classified as high risk. All patients had chemotherapy before surgery. Ninety study participants were treated with lumpectomy and 116 with mastectomy. Choice of surgical treatment and the use of post-operative radiation therapy were at the discretion of the treating physician. Patients were followed for an average of 3.9 years after diagnosis.
“Overall these high-risk patients had a low risk of local recurrence, but a significantly higher risk of tumor metastasis in other areas of the body,” comments Dr. Laura Esserman, Professor in the Departments of Surgery and Radiology and Affiliate Faculty of the Institute for Health Policy Studies, University of California, San Francisco Medical Center; Director of the Carol Franc Buck Breast Care Center; and Co-Leader of the Breast Oncology Program at the UCSF Helen Diller Family Comprehensive Cancer Center. “With today’s advanced treatments--which could include hormone therapy, chemotherapy and radiation depending on the patient--we found that distant metastatic cancers, not local recurrences, are the major risk for this patient population. Yet, many treatment plans provide aggressive therapies, such as mastectomy and radiation therapy, to prevent local recurrence in this patient group.”

Of the 206 patients enrolled in the study, only 14 patients (6.8%) had recurrences near the original tumor site, while 45 patients (21%) eventually developed cancers in other areas of the body. Tumor size and lymph node status at the times of diagnosis and of surgery were significantly associated with recurrence. Women who did not respond well to neoadjuvant chemotherapy, a sign of aggressive tumor biology, were also more likely to recur. Most significantly, local recurrence rates were not different in women who received lumpectomy compared to mastectomy.

Of the 14 women who had local recurrences, 10 also developed distant metastatic disease. “In this study,” notes Dr. Cureton, “local recurrence was closely associated with metastatic disease and seems to be another indication of aggressive tumor character, not the cause of the recurrence.”

Dr. Esserman adds, “This study has important implications for the treatment of women with high-risk breast tumors. Other portions of the I-SPY 1 trials confirmed that excellent tumor response to neoadjuvant chemotherapy and other pre-surgical treatments are strong predictors that the disease will not recur locally. Therefore, women who respond well to pre-surgical chemotherapy may not require other aggressive local treatment and may do well with a lumpectomy instead of mastectomy. This is a particularly important consideration when radiation is part of the treatment plan because radiation side effects are greater following mastectomy than lumpectomy. It also suggests that mastectomy without radiation should be investigated for appropriate high risk patients.”
Abstract

Serial #: 260

Title: Biology, not choice of mastectomy versus lumpectomy, dictates recurrence in high-risk breast cancer

Objectives: Increasingly, women with stage 2 and 3 breast cancers are receiving neoadjuvant therapy. At the completion of neoadjuvant therapy, the majority of women can have breast conservation. The question often arises in the setting of modern neoadjuvant therapy, is breast conservation oncologically safe even in the setting of residual disease. We used the experience of the I-SPY 1 trial to gauge the level of local recurrence in the setting of maximal multidisciplinary treatment.

Method: To be eligible for the I-SPY 1 trial, patients had to have tumors ≥3 cm. Women from 9 clinical centers received neoadjuvant doxorubicin and cyclophosphamide followed by paclitaxel followed by definitive surgical therapy, and then received radiation as deemed appropriate by the treating physician. To determine whether surgical procedure and type of response or lack thereof influenced the local recurrence rate, we separated the data into those with and without pathologic complete response (pCR) and by residual cancer burden (RCB) 0 or 1 versus 2 or 3 (complete or near complete response versus less complete response).

Results: Of the 236 patients enrolled in the I-SPY 1 trial, 206 were available for this analysis. Ninety-one % of patients in this trial were classified as biologically high risk on the basis of a 70-gene expression profile. The mean tumor size was 6.9 cm, and the tumors were 44% hormone receptor positive, 24% HER-2/neu positive and 32% triple negative. Median follow-up was 3.9 years. Of the 206 patients, 45 patients (21%) had a distant recurrence. However, only 14 patients (6.8%) had local recurrence (LR). Of the 14 that had a local recurrence, 9 (64%) had synchronous distant metastases and recurred 2 years of diagnosis, 1 had a metastasis within 2 years of local recurrence, and 4 have not had a distant recurrence. Developing a local recurrence was significantly associated with developing a distant recurrence (p=0.00005). Stage and size at clinical presentation and nodal status at operation after neoadjuvant chemotherapy were significantly associated with recurrence (p<0.0001, p<0.0001 and p=0.0006 respectively). Local recurrence rates were not statistically significantly different in women with lumpectomy compared to mastectomy, nor did they differ in the setting of an excellent response to therapy (pCR or RCB 0,1) or in the setting of residual disease (no pCR or RCB of 2,3). Tumor subtype certainly influences recurrence rate, but the number of local recurrences were too small to meaningfully evaluate the association.

Conclusions: Overall, these high-risk patients with maximal multidisciplinary treatment had a low risk of local recurrence, and those patients with higher risk of recurrence were those with more aggressive biological features such as lack of pathologic complete response. In this high-risk patient population, local recurrence does not appear to be a causative factor for future progression but rather an indication of aggressive tumor biology. When radiation is going to be part of treatment, lumpectomy may be associated with fewer complications than mastectomy, reconstruction and radiation treatment and should therefore be a consideration.