Risk Factors for Local Recurrence After Breast-Conserving Therapy

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NEW ORLEANS—In women treated with a breast-conserving approach for early-stage invasive breast cancer, “adequate” excision of the primary tumor is necessary to obtain optimal local tumor control. But what constitutes an adequate excision prior to radiation therapy, and what are the risk factors for local recurrence? A Harvard pathologist discussed this issue at the American Society of Breast Disease annual meeting.

Surgical procedures less than a gross excision result in unacceptably high local recurrence rates. However, the optimal extent of surgery needed beyond a complete gross excision has not been established. "Ideally, the surgical procedure should be large enough to ensure good local control but not so large that it compromises the cosmetic result," said James L. Connolly, MD, director of anatomic pathology, Beth Israel Deaconess Medical Center, and associate professor of pathology, Harvard Medical School.

The established risk factors for local recurrence include an incomplete excision and diffuse, malignant microcalcifications on mammography. Other relevant factors include patient age under 35; treatment factors such as extent of surgery, radiotherapy protocol, and addition of chemotherapy; and various tumor-related factors.

Presence of EIC

Many studies have investigated the relationship between the presence of an extensive intraductal component (EIC) and the risk of local recurrence after conservation. Despite differences in design, these studies have generally shown that invasive tumors with an EIC are associated with a significantly higher risk of local recurrence than tumors lacking an EIC, at least when information regarding the status of the microscopic margins is not available. Dr. Connolly said.

At Harvard, tumors with an EIC are defined as infiltrating ductal carcinomas that show the simultaneous presence of prominent ductal carcinoma in situ (DCIS) within the tumor (25% or more of tumor area and any DCIS adjacent to the tumor). This includes tumors that are predominantly DCIS with one or more microscopic foci of stromal invasion. Tumors lacking one or more of these features are categorized as EIC negative.

Harvard investigators have reported that EIC-positive tumors carry a 24% risk for local recurrence, compared with a 6% risk in EIC-negative tumors when margins were not evaluated. The vast majority of patients without EIC have low recurrence rates, Dr. Connolly said.

The Joint Center for Radiation Therapy, Boston, found that the likelihood of residual cancer was significantly higher in EIC-positive than in EIC-negative cancers, 88% vs 48% (P = .002). Moreover, in EIC-positive patients, most residual tumors were composed mostly of DCIS and were often widespread.

In EIC-negative patients, residual tumor typically consisted of only scattered microscopic foci of infiltrating cancer and/or DCIS. Other studies have made similar findings, he said, although the NSABP B-06 trial, which excluded patients with involved margins, found no adverse effect.

Dr. Connolly and his colleagues conducted a study in a mastectomy database to determine the relationship between EIC and the findings in the remainder of the breast. They found that 60% of EIC-positive tumors had residual tumor, compared with 30% of EIC-negative tumors. They also looked at the amount of prominent (about 3.6 cm) residual tumor and concluded that the vast majority of EIC-negative tumors were adequately treated with radiotherapy, but about 30% of EIC-positive cases contained too much residual tumor to treat in this manner. If you adequately excise these lesions, you can still treat them conservatively, he said. But some patients with...
EIC-positive tumors have too much breast involved for a good cosmetic result, and need a mastectomy.[]

In EIC-positive tumors, the associated intraductal involvement is often more extensive than can be appreciated clinically or at the time of surgery, Dr. Connolly said. Therefore, EIC-positive patients who undergo a limited resection of the clinically evident tumor frequently have considerable residual DCIS in the vicinity of the tumor site.[]EIC-negative patients, however, do not have high recurrence rates, so doing a large excision is a disservice to them,[] he commented.

Recent studies from Harvard and Stanford indicate that the presence of an EIC is not an independent predictor of local recurrence when the microscopic margin status is taken into consideration. Therefore, he added, EIC has evolved into more of a patient selection factor than a prognostic factor for local recurrence, helping to determine the extent of the surgical excision prior to radiotherapy. Perhaps the most important information from the pathologic exam is the status of the microscopic margins; however, margin status is always subject to sampling error.[]At our institution, we consider a margin positive when cancer cells (either invasive cancer or DCIS) abut the inked surface. If the tumor is not present at the inked surface, we report the smallest distance between the edge of the tumor and the inked tissue edge. This is done for both the invasive component and the associated DCIS,[[] he said.

Very wide excisions are probably not necessary in patients with negative margins, since they have a much lower recurrence rate. Dr. Connolly's most recent follow-up showed that local recurrence was only 7% in patients with negative margins or close margins. The risk for recurrence in patients with greater-than-focally-positive margins appears to be three times higher than in patients with focally positive margins. When greater-than-focally-positive margins is combined with EIC status, the risk is 19% in EIC-negative patients and 42% in EIC-positive patients.

Dr. Connolly added that the presence of margin involvement is not necessarily a contraindication to conservative surgery and radiation therapy. In many patients, negative margins can be obtained after re-excision. If prominent margin involvement persists in the re-excision specimen, however, mastectomy may be the most prudent approach, he said.

[]You should consider the location of the positive margins. If either the superficial margin or the deep margin abutting the pectoral fascia is involved, additional surgery is not necessary, since most of the breast tissue has been removed.

Additional factors that may affect local recurrence include lymphatic invasion, which is a factor in both EIC-negative and EIC-positive patients. Infiltrating lobular histology does not carry increased risk, and lobular carcinoma in situ appears not to be a risk factor for recurrence after breast conservation. Age less than 35 is also associated with an increased risk of local recurrence as well as distant metastasis.

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