Salpingo-Oophorectomy Cuts Female Ca Risks

In particular, the procedure lowers the incidence of breast cancer in women with BRCA2 mutations.

BY MELINDA TANZOLA
Contributing Writer

ATLANTA — Salpingo-oophorectomy appears to significantly reduce the incidence of gynecologic cancers in all women with BRCA mutations and the incidence of breast cancer in women with BRCA2 mutations.

This conclusion is based on the results of a multicenter, prospective study presented at the annual meeting of the American Society of Clinical Oncology.

After about 3 years of follow-up, the 546 women who elected to receive risk-reducing salpingo-oophorectomy had a 90% reduction in gynecologic cancers and a 47% reduction in breast cancer incidence compared with the 325 women who chose not receive surgery.

However, the risk reduction in breast cancer was limited to women with BRCA2 mutations. "BRCA1 and BRCA2 cause related but distinct cancer susceptibility syndromes," explained Dr. Noah D. Kauff in his presentation. He therefore thought it was important to examine the benefit of risk-reducing salpingo-oophorectomy in each population.

In all, 597 women with breast tissue at risk at the start of follow-up were included in the breast cancer risk analysis. Among women carrying the BRCA1 mutation, 15 of 190 patients treated with risk-reducing salpingo-oophorectomy developed breast cancer, compared with 19 of 178 patients not treated with surgery, a 39% risk reduction that was not statistically significant.

Among BRCA2 carriers, the incidence with surgery vs. surveillance was 4 of 113 patients and 9 of 116 patients, respectively, resulting in a significant 72% reduction in cancer risk.

The study, led by Dr. Kauff, of the Memorial Sloan-Kettering Cancer Center in New York, evaluated two prospective cohorts of women carrying a BRCA mutation. Compared with women who chose not to receive risk-reducing salpingo-oophorectomy, those treated with surgery were significantly older (mean age, 47 vs. 43 years), were more likely to have had breast cancer in the past (59% vs. 46%), were more likely to have taken hormone therapy (11% vs. 7%), and were significantly more likely to have given birth (83% vs. 74%).

An exploratory analysis showed an overall 78% risk reduction in estrogen receptor–positive cancer, compared with no significant change in the incidence of ER-negative breast cancer.

"Since most breast cancers related to BRCA1 mutations are ER-negative, it could be postulated that hormonal manipulation—in this case, risk-reducing salpingo-oophorectomy—might not be effective in this population," said Dr. Banu Arun in her discussion of the study.

Dr. Arun, of the department of breast medical oncology at the University of Texas M.D. Anderson Cancer Center, Houston, suggested that future prospective studies should evaluate risk-reducing salpingo-oophorectomy plus a nonhormonal preventive agent, such as cyclooxygenase-2 inhibitors, retinoids, statins, or other agents, for women with BRCA1 mutations. ■

Breast Ca Survival Aided by Early Switch to Aromatase Inhibitor

BY JANE SALODOF MACNEIL
Southwest Bureau

ATLANTA — Switching from tamoxifen to aromatase inhibitors improved overall survival for 8,794 breast cancer patients in four randomized phase III trials, according to a pooled analysis presented at the annual meeting of the American Society of Clinical Oncology,

Despite reporting benefits in progression-free survival, none of the individual published trials had shown that significantly more patients lived if they were switched to an individual aromatase inhibitor after 2-3 years of adjuvant hormonal therapy with tamoxifen.

'We were looking not for the effect of a single drug, but the effect of a class of drugs.'

DR. BRIA

Dr. Emilio Bria of Italy's Regina Elena National Cancer Institute in Rome and his coinvestigators found an absolute overall survival gain of 1.2% with aromatase inhibitors in the pooled data. They translated this into 100 patients who were cured as a result of the substitution.

Patients switched to an aromatase inhibitor had a relative risk of 0.76 for death from any cause, compared with patients who continued on tamoxifen. "We were looking not for the effect of a single drug, but the effect of a class of drugs," Dr. Bria said in an interview alongside the poster.

The pooled analysis only addressed an early-switch strategy because, Dr. Bria said, he could not find enough trials that have so far reported outcomes for upfront hormonal therapy with an aromatase inhibitor or for late switching to an aromatase inhibitor. The pooled trials compared continued tamoxifen use to initial tamoxifen followed by aminoglutethimide, exemestane, or anastrozole (J. Clin. Oncol. 2001;19:4209-15, N. Engl. J. Med. 2004;350:1081-92, J. Clin. Oncol. 2005;23:5138-47, Lancet 2005;366:455-62).

Other highly significant findings in the pooled analyses included a relative risk ratio of 0.67 for any event (local or distant relapse, secondary breast cancer, or death from any cause) in the aromatase inhibitor group, with an absolute benefit of 3.8% and a need-to-treat estimate of 26 patients to prevent one event.

The relative risk of recurrence was 0.68 with aromatase inhibitors, with an absolute benefit of 2.8% and a need-to-treat estimate of 36 patients.

For late recurrence, the relative risk was 0.64 and the absolute benefit was less than 1% with a need-to-treat estimate of 170 patients to prevent one death. (This was based on pooled data from 8,413 patients in three trials.) The relative risk of distant recurrence was 0.65 with aromatase inhibitors, with an absolute benefit of 2.4% and a need-to-treat estimate of 43 patients to prevent one death.

Patients switched to aromatase inhibitors were significantly more likely than patients who continued on tamoxifen to have fractures and musculoskeletal pain. The relative risk ratios were 1.50 and 1.33, respectively. Cardiovascular events also increased slightly, with a relative risk ratio of 1.22. Patients on aromatase inhibitors were, however, significantly less likely to have endometrial cancer (relative risk ratio 0.32) and somewhat less likely to have thromboembolic events (relative risk ratio 0.73). ■

Lymphadenectomy Extends Endometrioid Cancer Survival

BY SHARON WORCESTER
Southeast Bureau

ATLANTA — Lymphadenectomy improved survival in women with stage I, grade 3 through stage IV endometrioid uterine cancers in an analysis of more than 39,000 patients.

Although several studies have shown an association between lymphadenectomy and improved survival, questions remain about lymphadenectomy and staging, and whether there is a benefit for patients with stage I disease, said Dr. Nita Karnik Lee at the annual meeting of the American Society of Clinical Oncology.

The findings of the current study suggest lymphadenectomy performed during surgical staging is beneficial for women with stage I, grade 3 or higher endometrioid uterine cancers, Dr. Lee said.

The analysis focused on data from the U.S. National Cancer Institute's Surveillance Epidemiology and End Results (SEER) program during 1988-2001, including that from 12 registries. The data showed that of 39,396 women with endometrioid uterine cancers, 12,333 (31%) underwent surgical staging and lymphadenectomy. The remaining patients underwent hysterectomy and bilateral salpingo-oophorectomy without lymphadenectomy.

Overall 5-year disease-specific survival was 93% for stage I patients, 85% for stage II patients, 69% for stage III patients, and 38% for stage IV patients.

In the lymphadenectomy group, compared with the group without lymphadenectomy, 5-year disease-specific survival was 96% vs. 97% for those with stage I disease, 90% vs. 82% for those with stage II disease, 73% vs. 61% for stage III disease, and 52% vs. 28% for those with stage IV disease, said Dr. Lee, a clinical instructor at Stanford (Calif.) University Medical Center.

The differences were significant for those with stages II-IV disease, as well as for the subgroup of stage I patients with grade 3 disease. In this subgroup, 5-year disease-specific survival was 90% for those with lymphadenectomy vs. 85% in those without.

Also, in patients with deep myometrial invasion (stage IC, grade 3), there was a trend toward improved survival. The 5-year disease-specific survival was 82% in the lymphadenectomy group and 77% in the nonlymphadenectomy group; this difference was not statistically significant.

The proportion of patients with stage I disease was significantly higher in the group without lymphadenectomy (84% vs. 73%). In addition, there were about 20% more patients in the group without lymphadenectomy that had grade 1 disease. Perhaps consistent with these findings was the fact that this group received less radiation overall, compared with the lymphadenectomy group, she said.

On multivariate analysis, nonwhite race, advanced stage, advanced grade, and advanced age were prognostic factors associated with poorer survival. Year of diagnosis and presence of lymphadenectomy were independent prognostic factors associated with improved survival.

During a formal discussion of this study, Dr. Thomas Herzog of Columbia University, New York, noted that although it addresses the important question of the effect of lymphadenectomy on survival, the study is limited in a number of ways, including lack of randomization. Further, lymph node dissection was the only variable considered, minorities were underrepresented in the database, and the analysis fails to establish the role of lymph node dissection in all stage I cases, he added.

He said the methodological limits failed to answer critical questions, such as whether there is a threshold node count, whether there is value of lymphadenectomy in stage I patients, and whether the effect seen is a therapeutic or diagnostic effect, such as stage migration.

Nonetheless, the findings are consistent with guidelines released earlier this year regarding the role of lymphadenectomy in endometrioid uterine cancers, and they appear to help boost the level of evidence in support of these guidelines, he said. ■

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