Phila del phia — Adjuvant external beam radiation therapy with or without vaginal brachytherapy can lead to improved overall survival for some women with high-risk endometrial carcinoma, according to a study reported at the annual meeting of the American Society for Therapeutic Radiology and Oncology.

“Endometrial adenocarcinoma remains the most commonly diagnosed gynecologic malignancy in the United States, but optimal treatment for stage I and II disease remains controversial,” said Dr. Christopher M. Lee of the department of gynecologic oncology, Huntsman Cancer Hospital, Salt Lake City. He noted that selected high-risk subgroups have increased local-regional recurrence rates and decreased survival, but which of those patients might benefit from adjuvant radiation is still controversial.

In this retrospective analysis, Dr. Lee and colleagues utilized the National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) registry database to identify women with stage IC/grade 3 and stage II endometrial carcinoma without N1 or M1 disease. Specifically, they extracted data from the SEER 11 registries and Alaska data set containing data on patients diagnosed between 1988 and 2001. They identified 4,010 patients—all of whom had undergone hysterectomy with bilateral salpingo-oophorectomy—and analyzed prognostic factors such as age, race, cancer stage, tumor grade, extent of surgery, and whether or not they had received postoperative external beam radiation therapy (EBRT) with or without brachytherapy. Of the patients, 31.3% had received EBRT and 26.2% had received EBRT plus brachytherapy. “It was interesting to us that 42.5% of this population had received no further adjuvant treatment,” Dr. Lee said.

A Kaplan-Meier analysis revealed that patients with stage II/grade 1 disease received no additional survival benefit from either EBRT or brachytherapy alone or combined. However, patients with stage IC/grade 3-4, stage II/grade 2, and stage II/grade 3-4 disease all received additional benefit with EBRT plus or minus brachytherapy. “Of interest, there were significant improvements in overall survival between external beam radiation versus EBRT versus EBRT plus [brachytherapy] in both the stage IC high-grade and the stage II high-grade cohorts,” Dr. Lee said.

Further analysis revealed that older age, late diagnosis, black race, and no nodal exam at the time of hysterectomy all had a detrimental effect on survival. After controlling for these factors, the authors found that there was a significant overall survival advantage with EBRT plus or minus brachytherapy for patients with stage IC/grade 3-4, stage II/grade 2, and stage II/grade 3-4 disease, but not with stage II/grade 1 disease. Contrary to the prior results, there was no improvement in overall survival with the addition of brachytherapy to EBRT. These data show that “the improvement in overall survival is really due to the EBRT component” and not to the additional brachytherapy component,” Dr. Lee said.

Because of the retrospective nature of the trial, he cautioned against making too many conclusions about the data. “In the future, we would like to continue to look into and delineate the clinical and biological factors that would help us guide treatment and help us to account for the disparities we see between different patient cohorts, and to continue to develop a standardized and a risk-adaptive or stratified approach for adjuvant treatment for these patients,” Dr. Lee said.

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Ovarian cancer was the most common type of cancer among the patients in the study, accounting for 21 of 32 (66%) patients who enrolled in the clinical trial with the patient. The better a patient’s health was, as measured by her performance status, the more likely she was to participate. Of the patients with an initial Eastern Cooperative Oncology Group (ECOG) performance status of grade 0 (indicating a patient who is fully active), 59% chose to participate, compared with 51% of the patients with an initial performance status of grade 1 (indicating a patient who is able to carry out light or sedentary work). None of the patients with an initial performance status of grade 2 chose to participate in a trial.

Abnormal liver function tests also predicted nonenrollment in clinical trials. Among the factors that led to enrollment was no significant relationship between enrollment or nonenrollment were age, marital status, occupation, ethnicity, interval from diagnosis, number of previous surgical procedures or previous courses of radiotherapy, and the junior or senior physician status of the individual discussing the phase I trial with the patient.

Ovarian cancer was the most common type of cancer among the patients in the study, accounting for 21 of 32 (66%) patients who chose to participate in the clinical trials and 21 of 36 (58%) patients who chose not to participate. The majority of the remaining patients had cervical cancer. The patients participated in a wide variety of clinical trials, including those testing angiogenesis inhibitors, epidermal growth factor–receptor inhibitors, methyltransferase inhibitors, DNA repair inhibitors, and more.

“The practical limitations imposed by long-distance travel, together with the potential clinical benefit due to the participation in [phase I] trials, encouraged more investigators to develop phase I units in major cancer centers,” the investigators concluded.