RT and concurrent chemotherapy after surgery is effective treatment for high-risk endometrial cancer

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Radiation therapy with concurrent paclitaxel chemotherapy following surgery is an effective treatment for patients with high-risk endometrial cancer, according to a study published in the September 1, 2014 edition of the *International Journal of Radiation Oncology, Biology, Physics* (*Red Journal*), the official scientific journal of the American Society for Radiation Oncology (ASTRO).

Endometrial cancer is the most common gynecologic malignancy. Patients with early-stage disease are typically treated with surgery alone; however, patients with advanced endometrial cancer have higher instances of local or distant recurrence. Concurrent radiation therapy and chemotherapy after surgery is used to reduce the rate of recurrence in patients with advanced disease. This study, "A Phase 2 Trial of Radiation Therapy With Concurrent Paclitaxel Chemotherapy After Surgery in Patients With High-Risk Endometrial Cancer: A Korean Gynecologic Oncology Group Study," evaluates the efficacy and toxicity of concurrent chemoradiation with weekly paclitaxel in patients with stage III and IV endometrial cancer.

From January 2006 to March 2008, 57 patients from 20 institutions in Korea were included in the study. Patients eligible to participate in the study were between 20 and 80 years old, with a histologic diagnosis of International Federation of Gynecology and Obstetrics (FIGO) stage III or IV endometrioid adenocarcinoma with no history of prior surgery,

chemotherapy or radiation therapy for the treatment of other cancers. Patients with diagnoses of other cancers or severe infection requiring parenteral antibiotics, with a history of cardiac arrhythmia, congestive heart failure or myocardial infarction within the previous six months, or with uncontrolled infection, diabetes, hypertension or compromised cardiac, renal, liver or bone marrow functions were not included in the study. Of the 57 patients in this study, 12 patients (21.1 percent) had FIGO stage IIIA disease, 40 (70.1 percent) had FIGO stage IIIC disease and five (8.8 percent) had FIGO stage IV disease. Fourteen patients (24.6 percent) had grade 1 tumors, 27 (47.3 percent) had grade 2 tumors, and 16 (28.1 percent) had grade 3 tumors. The average age of the study patients was 52.2 years old.

All eligible patients had a staging laparotomy, including total abdominal hysterectomy, bilateral salpingo-oophorectomy (removal of both ovaries and both fallopian tubes), pelvic and para-aortic lymphadenectomy and peritoneal washing cytology. Patients in the study received a total dose of 45.0 to 50.4 Gy of external pelvic radiation therapy (1.8 to 2.0 Gy daily, five times a week), and 60 mg/m2 of paclitaxel diluted in 500 mL of 5 percent dextrose in water administered intravenously for three hours, once a week, for six weeks. Radiation therapy and chemotherapy were initiated within six weeks of surgery, and radiation therapy began either two days before or two days after the first chemotherapy treatment.

Chemotherapy was suspended due to adverse toxic effects in two patients. Of those two patients, one experienced septic shock, and one had persistent grade 4 neutropenia (an abnormally low count of neutrophils, a type of white blood cell) for more than two weeks. One patient refused treatment after enrollment, and two patients withdrew from treatment prior to completing all six cycles of chemotherapy. Fifty-two patients were included in the study's final analysis.

Patients received follow-up for five years after surgery. Chest X-ray and

abdominal-pelvic CT or MRI were conducted every six months for the first two years post-surgery and then annually for the next three years. Patients were also evaluated by pelvic examinations, monitoring CA125 blood serum levels and Papanicolaou tests every three months for the first two years post-surgery and then every six months for the next three years.

Severe toxicities observed during treatment were primarily hematologic toxicities. Of the 312 treatment cycles (52 patients each received six cycles), 52 episodes (16.7 percent) of grade 3 or 4 leukopenia (decrease in number of white blood cells) were observed, and 35 episodes (11.2 percent) of grade 3 or 4 neutropenia were observed. Hematologic toxicity caused 98 cycles to be delayed one week, and a paclitaxel dose reduction was required for eight patients (15.3 percent) who experienced persistent neutropenia for more than one week.

Disease recurrence occurred in 19 (36.5 percent) of the 52 patients in the final analysis. Eighteen patients (34.6 percent) experienced extrapelvic recurrence (lung, liver, bone, para-aortic, lymph node or other sites). One patient (1.9 percent) had intrapelvic recurrence in the vaginal vault. The median time to the detection of recurrence was 12 months (range 3 to 24 months).

Survival data was available for all 52 patients included in the analysis. By the end of the five-year follow-up period, nine patients (17.3 percent) had died of endometrial cancer. For all patients included in the study, the five-year disease-free survival rate was 63.5 percent (95 percent Confidence Interval (CI)), and the overall survival rate was 82.7 percent (95 percent CI).

"There is a lack of clear evidence on the best adjuvant treatment plan for patients with advanced endometrial cancer. There is growing evidence that chemotherapy should be administered to patients with advanced

disease in addition to radiation therapy," said Jae-Hoon Kim, MD, PhD, a co-author of the study, head of the department of obstetrics and gynecology at Gangnam Severance Hospital in Seoul, South Korea, and a professor in the Department of Obstetrics and Gynecology at Yonsei University College of Medicine in Seoul, South Korea. "This study shows that concomitant radiation therapy and weekly paclitaxel chemotherapy is a reasonable treatment option for patients with advanced endometrial cancer that can reduce toxicity and reduce pelvic recurrence. These favorable results should be further evaluated in a larger, prospective, randomized, controlled study to validate this treatment approach."

Provided by American Society for Radiation Oncology