



Randomized phase III trial of pelvic radiotherapy versus cisplatin-based combined chemotherapy in patients with intermediate- and high-risk endometrial cancer: A Japanese Gynecologic Oncology Group study

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Background

Randall et al.'s GOG study randomized stage III and IV patients to whole abdominal radiation vs. platinum-doxorubicin chemotherapy and demonstrated a hazard ratio for progression of 0.71 favoring chemotherapy. However, eliminating radiation must be done with caution given the high rates of pelvic recurrence in patients in whom radiation is omitted. One study study, GOG 156, attempted to randomize stage IB, IC, and II patients to pelvic radiation versus platinum-doxorubicin, but the study was closed due to poor accrual. This trial is the first to accrue adequate patients to address the question of whether chemotherapy is superior to pelvic radiation in intermediate and high risk endometrial cancer.

Methods

- The Japanese Gynecologic Oncology Group (JGOG) randomized 385 patients with stage IC-IIIC endometrial cancer with deeper than 50% myometrial invasion.
- Patients were excluded if they had received chemotherapy, radiation, or surgery previously for another cancer.
- Patients were required to be under 75 years old with an ECOG performance status of 0-3 and to have undergone total abdominal hysterectomy and bilateral salpingo-oophorectomy with no residual tumor.
- One hundred three institutions participated. Central pathology review was not performed.
- Radiation was delivered using opposed anterior and posterior fields to the whole pelvis to a dose of 45-50Gy in 4 to 6 weeks.
- Chemotherapy consisted of cyclophosphamide 333mg/m², doxorubicin 40mg/m², and cisplatin 50mg/m².
- The study was designed to have 80% power to detect a 13% difference in overall survival at a significance level of 5%.

Results

- Median follow-up was 60 months.
- Prognostic factors were well-balanced between study arms.
- 99% of patients assigned to radiation received at least 40 Gy. 97% of those assigned to chemotherapy received at least 3 cycles.
- 5% of patients receiving chemotherapy experienced a grade 3 or 4 toxicity versus only 2% of patients

receiving radiation. Most chemotherapy toxicity was myelosuppression.

- Important prognostic factors were similar to those demonstrated in other studies. Age ≥ 60 and histological grade ≥ 2 were the most important predictors of poor progression-free survival (PFS) and overall survival (OS).
- Patterns of relapse did not differ between arms.
- PFS and OS were the same in each arm.
- A subgroup analysis demonstrated superior PFS and OS in the chemotherapy arm for patients at high-intermediate risk of relapse but not for low-intermediate or high risk.
 - The low-intermediate risk group included stage IC patients under age 70 with grade 1 or 2 cancer.
 - The high-intermediate risk group included stage IC patients who were over age 70 or had grade 3 disease as well as patients with stage II or positive pelvic washings with $>50\%$ invasion of the myometrium.
 - The high risk group included stage IC patients over age 70 or having grade 3 cancer as well as patients with stage II or positive pelvic washings with $>50\%$ invasion of the myometrium.
 - The authors did not state whether the subgroup analysis had been planned prior to data collection.

Authors' Discussion

- Subgroup analysis is always limited.
 - In addition, the risk stratification used for subgroup analysis is different than that used in prior studies.
- Relatively low doses of doxorubicin may have contributed to low rates of complications in this trial.
 - GOG 107, 122, and 177 all delivered 60mg/m²
 - GOG 184 delivered 45 mg/m²

Reviewer's Discussion

- Chemotherapy appears to be reasonable treatment option for intermediate risk endometrial cancer. The number of high risk endometrial cancer patients in this trial was too few to draw definitive conclusions about their optimal treatment.

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