Interval Between Hysterectomy and Start of Radiation Treatment is Predictive of Recurrence in patients with endometrial carcinoma. A single Institution experience

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Background

- Endometrial cancer is the most common gynecologic malignancy in the U.S. and the second leading cause of gynecologic cancer death.
- Multiple randomized trials have shown a reduction in local recurrence with adjuvant radiation therapy for early stage endometrial cancer after hysterectomy.
- Data from other cancer sites suggests that the length of time between surgery and radiation can affect local control rates.
- The main goal of this study was to determine the impact of time interval between surgery and radiation on local control in patients with endometrial carcinoma FIGO Stage I-III.

Materials and Methods

- The prospectively-managed, UCARE database was queried, and 308 cases of early stage endometrial cancer treated between 1988 and 2010 were found.
- All patients received adjuvant radiation therapy, but no chemotherapy, after hysterectomy with at least one year of follow-up post-radiation therapy.
- All patients were fully staged at surgery with hysterectomy, bilateral oophorectomy, pelvic and para-aortic lymph node evaluation, and peritoneal cytologic sampling.
- Tumor grade, stage, and tumor size were also recorded in the database.
- Time interval between surgery and radiation was analyzed both as a continuous variable and dichotomous categorical variable.
- The impact of time interval on relapse-free survival (RFS) was calculated.
- Multivariate modeling was performed to identify predictors of local recurrence.

Results

- Mean age of the cohort was 64.78 years.
- The majority of patients were white and with endometroid histology. 93% had negative cytology and 41% had lower uterine segment involvement.
- Nearly 90% of patients were stage IA, IB, and II, but 10% of the cohort was stage III.
- 20% of patients had external beam radiation alone, 27% had vaginal cuff brachytherapy alone, and the remainder had combined therapy.
- The patients were divided into two groups based on the time interval between surgery and radiation, < 9 weeks (n=269) and > 9 weeks (n=39).
- Overall recurrence was lower in the shorter time interval group, 9.3% vs. 46.2% and the difference was statistically significant.
- Vaginal, pelvic, and distant recurrences were all significantly higher in the longer time interval group.
- 5-year RFS was 90% in the shorter time interval group vs. 43% in the longer time interval group, and this result was statistically significant.
- On multivariate analysis, delay of RT to nine weeks or more (p=<0.001), the presence of lymphovascular space involvement (p=0.001), higher FIGO grade (p=0.012) and cervical stromal involvement (p=0.046) were independent predictors of tumor recurrence.

**Author's conclusions**

- Delay in administration of radiation therapy greater than 9 weeks following hysterectomy was associated with an increased risk of disease recurrence.
- A shorter time interval between surgery and radiation therapy may be beneficial.

**Clinical Implications**

- Endometrial cancer is prevalent in the U.S., and radiation therapy plays an important role in management after hysterectomy.
- The goal of this study was to determine if time interval between surgery and radiation has an effect on relapse free survival.
- Prior studies of cervical cancer and head and neck cancer have demonstrated that total "package time," or time from initiation of surgical treatment to completion of radiation therapy, has an impact on local control.
- This study demonstrated that time interval between surgery and radiation had a significant impact on RFS for early stage endometrial cancer.
- In general, package time has been demonstrated to be of importance in squamous cell carcinomas and other rapidly growing tumors such as lymphomas. Studies of other sites with adenocarcinoma histology, such as prostate cancer, have generally not shown such a dramatic effect of total package time.
- Of note, the authors included tumor characteristics such as grade and size in the analysis, but did not include patient factors such as age. Evidence from the PORTEC studies demonstrates that age is an important prognostic factor and is predictive of local recurrence. Omission of age in the analysis may have skewed the results.
- Nonetheless, this study highlights an important area for further study. If the time interval between surgery and radiation therapy does indeed influence local control to the magnitude observed in this study, multidisciplinary collaboration will be needed to ensure that patients are referred and start radiation in a timely fashion.