Current Management of Stage I Adenocarcinoma of the Endometrium

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Abstract

Objective: This study was undertaken to assess the current management and outcome of patients with stage I adenocarcinoma of the endometrium.

Methods: One hundred thirty-five patients with stage I adenocarcinoma of the endometrium were treated with hysterectomy, bilateral salpingooopherectomy, and surgical staging. Patients were then stratified into high risk or low risk groups based on grade, depth of myometrial invasion, and the presence or absence of lymphvascular space invasion. Postoperative treatment was then individualized based on risk assessment.

Results: Sixteen of 135 patients (12%) underwent postoperative adjuvant pelvic radiation. The remaining patients were treated with observation following surgery. Actuarial survival at three years was 97%.

Conclusions: Surgical staging of endometrial cancer provides critical information with regard to the extent of cancer and prognosis. When cancer is confined to the uterine corpus, histopathologic findings can be used to assess individual patient risk; high risk patients may then be selected for postoperative radiation. Relatively few patients will require adjuvant treatment and overall survival appears excellent.

Introduction

The primary treatment for adenocarcinoma of the endometrium generally involves total hysterectomy and bilateral salpingooopherectomy. In 1988 the International Federation of Gynecology and Obstetrics (FIGO) modified the staging of endometrial cancer from a clinical to a surgical staging system. This clearly provides a better assessment of the extent of disease; this knowledge then allows for more individualized therapy. Patients with extrauterine disease or with identifiable risk factors may then be selected for postoperative radiation or more aggressive therapy. Unnecessary treatment may be avoided in the low risk patient.

Frequently, however, women with endometrial cancer undergo hysterectomy and salpingooopherectomy without the benefit of regional lymphadenectomy and surgical staging. Perioperative radiotherapy is then administered at the discretion of the individual physician. Treatment approaches, therefore, may vary considerably, depending upon personal experience and anecdotal evidence. Utilization of adjuvant treatment may be inconsistent and result in overtreatment or undertreatment of individual patients.

The present study, therefore, was undertaken to review a series of consecutive patients with FIGO stage I adenocarcinoma of the endometrium. Patients in this series were surgically staged, then stratified into high risk and low risk groups based on histopathologic findings. Postoperative radiotherapy was then administered based on risk category. This study reports on the results of treatment.

Materials and Methods

Patients with stage I adenocarcinoma of the endometrium were identifed through The Queen's Medical Center tumor registry. All patients treated by the author from July 1989 through December 1995 were identified. Patient information and pathologic findings were abstracted from patient records. 135 consecutive patients with surgical-pathologic stage I carcinoma were identified and included in the study.

All patients underwent hysterectomy and bilateral salpingooopherectomy, including two patients who underwent radical hysterectomy and ten who underwent laparoscopic vaginal hysterectomy. 101 patients underwent selective pelvic lymphadenectomy and 14 patients underwent selective paraaortic lymphadenectomy. There were 30 patients that had grade 1 or 2 tumors grossly confined to the endometrium at the time of surgery that did not undergo staging lymphadenectomy. In addition there were 4 patients that did not undergo staging lymphadenectomy because of various medical or technical contraindications. No patients received preoperative radiation; all patients with disease documented beyond the uterine corpus were excluded from this series.

There were 124 patients with endometrioid adenocarcinoma and 11 with papillary serous or clear cell histology. Lymph-vascular space invasion was found in 16 patients. Table 1 summarizes findings regarding substage and grade.

Table 1.— Tumor grade stratified by substage.

Grade	Substage			
	IA	IB	IC	Total
1	42	17	1	60
2	16	22	8	46
3	6	13	10	29
Total	64	52	19	135

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Patients were stratified into high risk and low risk groups based on the presence of three factors: (1) grade 3 tumor, (2) stage IC (greater than 50% myometrial invasion), and (3) the presence of lymph-vascular space invasion. Papillary and clear cell carcinoma were included in the grade 3 category. Patients with 0 or 1 risk factor present were considered low risk; patients with 2 or 3 risk factors present were considered high risk. Life table analysis was used to calculate survival and chi-square was used as a test of statistical significance. Postoperative radiotherapy was administered according to histopathologic findings and risk category. Radiotherapy consisted of external radiotherapy (45Gy) to the whole pelvis followed by a single intracavitary application of vaginal colpostats.

Results

There were 15 patients in the high risk category and 120 patients in the low risk category. Sixteen of 135 patients (12%) received postoperative radiation. All patients in the high risk group were referred for radiation; three patients in this group declined treatment. Four patients in the low risk group did not undergo staging lymphadenectomy and were treated with radiation; two patients with stage IB papillary serous carcinoma, and two patients with stage IB grade 3 adenocarcinoma. Actuarial survival for the entire group at three years was 97%. Survival for the low risk group was 98%, and 85% for the high risk group at three years. The difference in survival between the low risk and high risk groups was statistically significant (p < .05).

Ten patients developed recurrent disease. Two patients in the high risk group (13%) developed distant metastases and died of their disease. Seven patients in the low risk group (5.8%) developed local (ie. vaginal) recurrences. These were all treated with radiation. Four of these patients remain free of disease; one has been lost to follow-up; two have died of their cancer. Both patients that died of local recurrence had persistent local disease following radiation. There was one distant failure in the low risk group; this patient had one risk factor present (high grade). The two high risk patients with distant metastases presented with all three risk factors present. Of the seven with local recurrences, six had no risk factors present; one had stage IB clear cell carcinoma. Although all local recurrences occurred in the low risk group, this was not statistically significant (p > .05). The incidence of distant metastases, however, was significantly higher in the high risk group (p < .05).

In this series there were 28 patients with one risk factor present. Four did not undergo staging lymphadenectomy because of medical or technical reasons; these four were treated with postoperative radiation. The remaining 24 were surgically staged and treated with observation alone following hysterectomy. Of these 24 patients there was one local recurrence (4%) and one distant recurrence (4%).

Discussion

Carey et al.[1], in 1995 reported on a series of 384 patients with clinical stage I adenocarcinoma of the endometrium. In this series low risk patients were defined as grade 1 or 2 with less than 50% myometrial invasion. Adjuvant radiotherapy was not utilized for low risk patients and five year survival was 95%. Patients with deep myometrial invasion or high grade tumors were generally treated with postoperative radiation. Forty-one percent of patients received

adjuvant radiation; survival at three years for the high risk group was 81% and overall survival for the entire series was 92%. In the present series 12% of patients received radiation and overall survival at three years was 97%. This series utilizes surgical staging and therefore a different classification scheme. The presence of high grade, deep myometrial invasion, and/or lymph-vascular space invasion were used to stratify patients: patients with 0 or 1 risk factor present were low risk, and patients with 2 or 3 risk factors were high risk. This scheme assigns select 'high' risk patients with negative lymph nodes into the low risk category: stage IC grade 1,2 cancer, stage IA or B grade 3 cancer, and patients with stage IB grade 1 or 2 cancer with lymph-vascular space invasion. With surgical staging and negative regional nodes, the recurrence risk in this group appears low. There were 24 of these patients who did not receive postoperative radiation; there was one local recurrence and one distant recurrence. Of the 91 patients with no risk factors present there were six local recurrences (5%) and no distant recurrences. Three year survival for entire low risk group was 98%.

Kadar et. al.[2] reported similar findings in 262 patients who were similarly stratified by grade, depth of myometrial invasion, lymph-vascular invasion, and cervical stromal invasion. Of 220 patients with 0 or 1 risk factor present, 27% underwent postoperative radiation and 5 year survival was 97%.

There is some question as to whether low risk patients benefit from postoperative vaginal brachytherapy to prevent local recurrence. Piver et. al.[3] reported no local recurrences in 90 low risk women treated with hysterectomy and postoperative vaginal brachytherapy. Kucera[4] reported a local recurrence rate of 0.8% in a similarly treated group. In Carey's series the incidence of local recurrence in low risk patients treated with surgery alone was 2.6% with an associated mortality of 1.3%. Elliott et. al[5] reported a 4.9% incidence of local recurrence in low risk patients treated with surgery alone. The incidence of local recurrence in the present series is similar (5.8%); with a mortality of 1.6%. It would appear, therefore, that postoperative vaginal brachytherapy in all low risk patients may reduce the risk of a fatal local recurrence by 1-2%. It is difficult to assess whether this represents a meaningful decrease in mortality. Certainly any major complications resulting from the routine use of brachytherapy would obviate any marginal improvement in survival.

Ackerman et. al.[6] reviewed 54 patients with recurrent endometrial cancer. Eleven of 14 patients (79%) with vaginal vault recurrences confined to the vaginal mucosa were controlled with pelvic radiation at the time of relapse. Therefore in low risk patients, withholding radiation until the time of relapse appears to be a reasonable option. It bears emphasis, however, that as vaginal vault recurrences are not uncommon and have a reasonable likelihood of salvage, these patients should be monitored quite closely in the postoperative period.

The postoperative management of high risk patients remains more problematic. Postoperative pelvic radiation appears to result in excellent local control, however these patients remain at significant risk for systemic failure. A number of studies[7,8,9] have failed to demonstrate a survival benefit for high risk patients undergoing postoperative pelvic radiation. Pelvic radiation may simply alter the pattern of recurrence rather than significantly impacting survival. There is an ongoing trial sponsored by the Gynecologic Oncology

Group randomizing high risk Stage I patients to postoperative radiation versus systemic chemotherapy. The results of this trial should yield valuable information regarding the adjuvant treatment of high risk patients.

In summary, the surgical staging of endometrial cancer provides vital information with regard to the extent of cancer and ultimate prognosis. When cancer is confined to the uterine corpus histopathologic findings can be used to stratify patients into high risk and low risk groups. Postoperative therapy can then be tailored to the individual patient.

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