Pelvic Exenteration for Recurrent Endometrial Cancer

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Pelvic exenteration is generally not considered an operation with curative value for women with recurrent endometrial carcinoma. We reviewed our experience with pelvic exenteration performed in patients with recurrent endometrial adenocarcinoma from 1947 through 1994. A total of 44 patients were identified, with a mean age of 60 years (range 35–69 years). Primary therapy usually consisted of total abdominal hysterectomy with bilateral salpingo-oophorectomy, with most receiving either pre- or postoperative radiotherapy. Prior to exenteration, 10 of 44 (23%) patients had never received any form of radiotherapy. The median interval between initial surgery and exenteration was 28 months (range 2–189 months). The type of exenteration performed was total in 23 patients (52%), anterior in 20 patients (46%), and posterior in 1 patient. Major postoperative complications occurred in 35 patients (80%) and included urinary/intestinal tract fistulas, pelvic abscess, septicemia, pulmonary embolism, and cerebrovascular accident. Median survival for the entire group of patients was 10.2 months. Nine patients (20%) achieved long-term survival (>5 years). Pelvic exenteration for recurrent endometrial cancer is associated with a high operative morbidity and poor overall survival. Although only 20% of patients achieved long-term survival, this procedure remains the only potentially curative option for the few patients with central recurrence of endometrial cancer who have failed surgical and radiation therapy.

INTRODUCTION

Endometrial adenocarcinoma is the most common gynecologic malignancy and is characterized by early diagnosis and long-term survival for most patients. Standard therapy is hysterectomy, bilateral salpingo-oophorectomy, and, in select patients, lymph node sampling. Recurrence, although relatively uncommon, is usually associated with disseminated disease and is not easily treatable with secondary surgical procedures or radiotherapy. Less commonly, endometrial cancer recurs locally in the vaginal apex or the vaginal tube itself [1, 2]. These women are candidates for vaginal and pelvic radiotherapy. However, if these women have already received radiation therapy, their treatment options are limited. Pelvic exenteration is a viable treatment option for this subset of women.

Pelvic exenteration is usually reserved for the treatment of central recurrence of endometrial cancer. Few studies have examined the role of pelvic exenteration for recurrent endometrial cancer, and of those, published cure rates are generally lower than for cervical cancer [3, 4]. Therefore, women are rarely considered for exenteration as a cure for recurrent endometrial cancer.

Our study revisits the role of pelvic exenteration in the treatment of women with central recurrence of endometrial adenocarcinoma.

MATERIALS AND METHODS

We performed a retrospective chart review of 44 patients with recurrent endometrial adenocarcinoma who underwent a pelvic exenterative procedure at our institution between 1947 and 1994. The exenterative procedures were performed more frequently in the earlier years of the study, with 4 patients undergoing the procedure in the 1940s, 21 in the 1950s, 13 in the 1960s, 3 in the 1970s, 2 in the 1980s, and only 1 in the 1990s.

In 37 patients the initial clinical stage was not recorded. Using the clinical pre-1988 FIGO staging criteria, 2 patients had Stage I disease, 1 patient had Stage II disease, and 3 patients had Stage III disease. One patient had Stage I disease using the post-1988 staging criteria.

Forty patients underwent abdominal hysterectomy as part of their initial treatment. Of these 40 patients, 16 patients also received perioperative radiation therapy: 5 patients received preoperative radiation therapy, 10 patients received postoperative radiotherapy, and 1 patient had received a combination of radiation and chemotherapy postoperatively. Two of the 40 patients had received prior chemotherapy.

Only 3 patients had pelvic lymphadenectomy at the time of their initial surgery, and none of the patients had para-aortic lymph node sampling. The histologic grade of the tumor was known in 12 of the 44 patients: grade 1 in 3, grade 2 in 6, grade 3 in 1, and grade 4 in 2. The depth of myometrial invasion was known in only 2 patients (both <50%). All patients had re-
moval of all gross disease at their initial surgery. Four patients had pelvic radiotherapy as their primary treatment. The dose of radiotherapy was unavailable for most patients.

After initial tumor recurrence, 14 patients were treated with other limited surgical procedures, radiation therapy, chemotherapy, or hormonal therapy prior to undergoing pelvic exenteration. Ten patients never received any form of adjuvant therapy prior to exenteration.

Survival curves were estimated using the Kaplan–Meier product limit estimates and compared using the log rank test [5, 6].

RESULTS

Of the 44 patients undergoing pelvic exenteration, 23 were treated with a total pelvic exenteration, 20 had an anterior exenteration, and 1 underwent a posterior exenteration. No patients received intraoperative radiotherapy. Seven patients had metastasis to pelvic lymph nodes, and 2 patients had metastasis to the para-aortic lymph nodes. As these patients were considered to be curable with aggressive treatment, they underwent an exenterative procedure. The remaining 35 patients had no lymph node metastases.

Histologic grading at the time of pelvic exenteration revealed one moderately differentiated adenocarcinoma, five poorly differentiated adenocarcinomas, four anaplastic lesions, two with papillary-serous adenocarcinoma, and one with mucinous adenocarcinoma. In the remaining patients, the histologic grade could not be determined.

The median patient age at the time of exenteration was 60 years (range 35–69). The mean length of time from initial surgery to pelvic exenteration was 28 months (range 2–189 months). Eight patients underwent exenteration within 1 year of initial diagnosis, eight patients at 12–24 months, nine patients at 24–36 months, two patients at 36–48 months, and six patients at 48–60 months from the time of initial diagnosis. Seven patients recurred greater than 5 years after their initial diagnosis. Two patients underwent exenteration 6 years after initial diagnosis, two patients at 7 years, one patient at 8 years, one patient at 14 years, and one patient at 16 years after initial diagnosis. There was no significant difference in survival related to time of recurrence.

The median operative time was 240 min, with a median estimated blood loss of 3138 cm³. Vaginal reconstruction was not routinely performed at the time of exenteration. Intraoperative surgical complications, including vascular and bowel injuries, occurred in 7 patients (16%). Of these complications, 1 vascular injury caused the only intraoperative death. Thirty-five of the 44 patients (80%) experienced major postoperative complications. These included 3 patients with gastrointestinal fistulae, 4 with urinary fistulae, 4 with hyperchloremic acidosis, 4 with prolonged paralytic ileus, 3 with pelvic abscesses, 2 with pneumonia, 3 with pyelonephritis, 2 with wound dehiscence, 2 with wound infection, 2 with congestive heart failure, 2 with leg cyanosis, and 1 each with pleural effusion, pulmonary edema, peritonitis, hemolytic jaundice, gram-negative bacteremia, cerebrovascular accident, deep-venous thrombosis, and severe depression. The median length of stay in the hospital postoperatively was 33 days (range 6–109 days). Six patients died in the immediate postoperative period. Two patients died of pulmonary embolism, 1 died of a cerebrovascular accident, 1 experienced pulmonary edema and peritonitis, 1 died from peritonitis, and 1 died from septicemia and hemolytic jaundice.

During the follow-up period, 24 patients died within 1 year of the exenterative procedure and 4 patients died in the second year after the procedure, all of recurrent disease except for 3 patients who died of other causes. Using the Kaplan–Meier product limit method, the overall median survival was 10.2 months (CI 7–23 months) (Fig. 1). There was no significant difference in survival in those patients who had received radiation therapy prior to exenteration compared to those who had not received radiation therapy (Fig. 2). Nine patients achieved long-term survival greater than 5 years. Five patients, including 1 patient with positive lymph node metastasis, survived greater than 10 years after exenteration. Three died secondary to other causes at 19 years, 21 years, and 22 years after exenteration.

Interestingly, two of the nine long-term survivors had positive metastatic disease in the pelvic lymph nodes. These two patients died at 62 and 176 months after exenteration, respectively.

DISCUSSION

Once endometrial cancer has recurred, the treatment options are quite limited. Most women have undergone both surgical and radiation therapy, and chemotherapy has not added significantly to long-term survival [7–10]. Doxorubicin in doses of 50 to 65 mg/m² has been associated with an overall response rate of 26% [7], which is similar to the reported rate of 25% with single-agent cisplatin [8]. Combining cisplatin with doxorubicin resulted in a higher response rate than doxorubicin alone; however, overall survival was no different [9]. In a GOG Phase II trial, 30 patients with advanced or recurrent endometrial cancer, not treated with prior chemotherapy, were treated with single-agent paclitaxel. Although the overall response rate was 36%, the complete response was only 14% [10]. Chemotherapy is a viable treatment option; however, its effect on long-term survival is limited. Progestational agents can result in a 25% response rate in patients with recurrent disease; however, the average time to progression is only 4 months [11].

Pelvic exenteration represents the only potentially curative option for patients with centrally recurrent endometrial cancer. Barber and Brunschwig [3] reported on 36 patients who underwent pelvic exenteration for recurrent endometrial adenocarcinoma. Disease was localized, however, in only 5 (14%) of the patients. Their overall 5-year survival rate was reported to
be 14%, with a postoperative complication rate of 61%. The authors concluded that although limited, there was a role for pelvic exenteration in the management of women with recurrent endometrial cancer. Morris et al. [4] reported on 20 patients who underwent pelvic exenteration for recurrent endometrial cancer between 1955 and 1988 at four major institutions. They reported an absolute 5-year survival rate of 45%, with a complication rate of 60%. The current series reports similar complication rates but lower survival in a single institution experience with a larger number of patients treated during a similar time period.

The subset of women that are candidates for pelvic exenteration for recurrent endometrial cancer is highly specific. Because of the disseminated nature of recurrent disease, most women who recur will not be eligible for the procedure. Prior to being considered a candidate for exenterative surgery, patients must undergo a full evaluation to rule out metastatic disease, including diagnostic imaging with CT of the chest, abdomen, and pelvis. MRI of the pelvis may be useful in detecting pelvic side wall involvement and can further reduce the number of patients undergoing unnecessary exploration. At the time of exploration, patients with intra-abdominal metastases, positive lymph nodes, or tumor fixed to the pelvic side wall are not considered candidates for exenteration. As noted by Jones [12], the survival of patients with positive pelvic nodes undergoing exenteration for cervical cancer is less than 10%. Since nodal metastasis likely represents systemic disease, one could assume that the same holds true for endometrial cancer. The availability of modern imaging techniques has undoubtedly reduced the number of patients with recurrent endometrial cancer being explored for exenteration. Unlike cervical cancer, in which disease recurrence is more likely to be localized, endometrial cancer tends to recur in the upper abdomen or at distant metastatic sites such as lung or liver. It is thus much rarer for exenteration to be employed for this group of patients, as noted in the current series in which only three of these procedures were performed at our institution over the past 2 decades.

Pelvic exenteration in our study carries a high morbidity and an overall poor prognosis (20%). The high mortality rate noted
in our experience may reflect the fact that the majority of cases were performed before 1980, prior to the availability of modern antibiotics and intensive care units. Currently, it represents the only option for potential cure in the rare patient with central recurrence of endometrial cancer after undergoing surgical and radiation therapy.

REFERENCES