Pelvic exenterations for advanced and recurrent endometrial cancer: clinical outcomes of 40 patients

Schmidt, Ana-Maria; Imesch, Patrick; Fink, Daniel; Egger, Herwig

Abstract: OBJECTIVE The aim of this study was to analyze the clinical experience and outcome of patients who have undergone pelvic exenteration for primary advanced or recurrent endometrial cancer. METHODS We analyzed the medical records of 40 women who underwent pelvic exenteration to treat primary advanced or recurrent endometrial cancer. RESULTS Pelvic exenteration was performed in 40 patients with primary advanced or recurrent endometrial cancer. Three patients (8%) underwent a primary exenteration, and 37 patients (92%) underwent a secondary exenteration. A total exenteration, anterior exenteration, and posterior exenteration was performed in 85%, 5%, and 10% of patients, respectively. In 31 cases, exenteration was performed with a curative aim, and in 9 cases, exenteration was performed with a palliative aim. The overall survival rates were 61.4% at 5 years and 51.1% at 10 years. For the 31 patients who underwent pelvic exenteration with a curative aim, the overall survival rates were higher than those for the entire study population and were 72.6% at 5 years and 59.4% at 10 years. For the 9 patients who underwent a palliative exenteration, the overall survival rates were 19.1% at 5 years and 0% at 10 years. This is to the best of our knowledge the biggest study of pelvic exenteration in patients with endometrial cancer. CONCLUSIONS Our data show that pelvic exenterations are a valid therapeutic option with long-term survival in select patients.

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Pelvic Exenterations for Advanced and Recurrent Endometrial Cancer: Clinical Outcomes of 40 Patients

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Objective: The aim of this study was to analyze the clinical experience and outcome of patients who have undergone pelvic exenteration for primary advanced or recurrent endometrial cancer.

Methods: We analyzed the medical records of 40 women who underwent pelvic exenteration to treat primary advanced or recurrent endometrial cancer.

Results: Pelvic exenteration was performed in 40 patients with primary advanced or recurrent endometrial cancer. Three patients (8%) underwent a primary exenteration, and 37 patients (92%) underwent a secondary exenteration. A total exenteration, anterior exenteration, and posterior exenteration was performed in 85%, 5%, and 10% of patients, respectively.

In 31 cases, exenteration was performed with a curative aim, and in 9 cases, exenteration was performed with a palliative aim. The overall survival rates were 61.4% at 5 years and 51.1% at 10 years. For the 31 patients who underwent pelvic exenteration with a curative aim, the overall survival rates were higher than those for the entire study population and were 72.6% at 5 years and 59.4% at 10 years. For the 9 patients who underwent a palliative exenteration, the overall survival rates were 19.1% at 5 years and 0% at 10 years. This is to the best of our knowledge the biggest study of pelvic exenteration in patients with endometrial cancer.

Conclusions: Our data show that pelvic exenterations are a valid therapeutic option with long-term survival in select patients.

Key Words: pelvic exenteration, endometrial cancer, survival, radical surgery

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The aim of this study was to analyze the outcome of patients who have undergone pelvic exenteration for primary advanced or recurrent endometrial cancer. These patients are normally older than patients with cervical cancer and, therefore, often have numerous comorbidities. Thus, the decision to perform pelvic exenteration is made highly restrictively. Our data indicate that despite of these problems, pelvic exenteration for primary advanced or recurrent endometrial cancer is an option that is feasible with high survival rates and, therefore, should be considered as a treatment option for these patients.

PATIENTS AND METHODS

We retrospectively analyzed the medical records of 40 patients who underwent pelvic exenteration because of primary advanced or recurrent endometrial cancer.

Exenteration was indicated as the primary treatment when the uterine tumor had infiltrated the bladder and/or rectum inducing fistulas. Most cases were secondary exenterations performed after an initial operation with or without irradiation treatment; in those cases, the indication for exenteration was tumor recurrence that met the criteria for primary exenteration.

All 40 patients underwent a preoperative examination under general anesthesia to verify the presence of a tumor histologically and to evaluate the tumor’s operability. This examination also included a cystoscopy and rectoscopy. In addition, a computerized tomography scan was performed.

If the computerized tomography scan showed no evidence of metastasis, no intra-abdominal metastases were found during the operation and clear margins were pathologically confirmed, the exenteration was considered curative. An exenteration was considered palliative in cases with distant metastasis, a positive lymph node metastases; for the remaining patient, no histological record was found.

Among 40 patients, 12 women (30%) had comorbidities, including 4 with hypertonia, 2 with diabetes or severe obesity, 1 with nicotine abuse, and 3 with multiple comorbidities (Table 1). All exenterations were performed at the Department of Gynecology of the General Hospital Neumarkt and the Department of Gynecologic Oncology of the University Hospital Erlangen. In total, 7 surgeons were involved in this study.

Anterior exenteration was defined as the removal of the uterus and vagina with the bladder, the pelvic ureters, and the urethra, and posterior exenteration was defined as the removal of the reproductive tract with the rectosigmoid colon. Total exenteration included the removal of both the anterior and posterior compartments.

Reconstruction included the formation of a continent ileocolic bladder (30/40) whenever possible; otherwise, conduits (4/40) and uretero-uretero-stomas (2/40) were constructed. In addition, 30 colonic neovaginas were generated using the caudal 10 cm of the colon above the resection. This portion of the colon was divided from the rest of the colon to preserve its blood supply and was then rotated 180 degrees. Furthermore, the omental flap was used in 32 cases to provide much better pelvic filling, and this reduced the specific morbidity. Of 40 patients, 31 (78%) received complete continent reconstruction.

To restore bowel continuity, 37 colorectal or coloanal anastomoses were performed. In cases with high irradiation doses or extremely deep anastomosis, a temporary protective stoma was built for 6 weeks (16/40). Three patients required a permanent colostomy.

The survival analysis was performed using Kaplan-Meier curves and Greenwood 95% confidence bands. Survival curves were compared using the log-rank test. Fisher exact test was used to examine the significance of the association between 2 variables in a $2 \times 2$ contingency table.

RESULTS

Pelvic exenteration was performed in 40 patients with primary advanced or recurrent endometrial cancer. Three patients (8%) underwent a primary exenteration, and 37 patients (92%) underwent a secondary exenteration. For the secondary exenteration cases, the disease-free period from initial treatment to the time of exenteration ranged from 4 to 111 months, with a median of 24 months, and 32% (12/37), 3% (1/37), and 65% (24/37) of those patients had been pretreated with surgery alone, irradiation alone, and a combination of surgery and irradiation, respectively. Two patients in the latter group also received chemotherapy. Of the 36 patients who were surgically pretreated, 13 underwent lymphadenectomy, and of those 13 patients, 9 were nodal negative and 3 had lymph node metastases; for the remaining patient, no histological record was found.

Of 40 patients included in this study, 2 (5%), 4 (10%), and 34 (85%) underwent an anterior, posterior, and total exenteration, respectively. In 31 cases (78%), exenteration was

<table>
<thead>
<tr>
<th>TABLE 1. General demographics for the cohort</th>
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<tbody>
<tr>
<td>General demographics</td>
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<tr>
<td>Age (43–55 y)</td>
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<tr>
<td>Age (56–64 y)</td>
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<tr>
<td>Age (&gt;65 y)</td>
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<tr>
<td>Obesity</td>
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<tr>
<td>Diabetes</td>
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<tr>
<td>Vascular diseases</td>
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<tr>
<td>Others or combination of diseases named previously</td>
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<tr>
<td>Curative exenteration</td>
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<td>Palliative exenteration</td>
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<td>Primary exenteration</td>
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<tr>
<td>Secondary exenteration</td>
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<td>Interval pretreatment/ exenteration</td>
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<tr>
<td>After initial operation (12 patients)</td>
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<tr>
<td>After initial radiation (1 patient)</td>
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<td>After initial operation and radiation (24 patients)</td>
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performed with a curative aim, and in 9 cases (23%), exenteration was performed with a palliative aim.

The median patient age was 63.5 years with a range of 43 to 78 years. The mean follow-up time after exenteration was 51 months, with a median of 35 months and a range of 1 to 263 months.

A lymphadenectomy was performed in 37 patients, and 3 patients in the secondary exenteration group had not undergone a lymphadenectomy. There were 2, 4, and 31 patients who had undergone pelvic, para-aortic, and both pelvic and para-aortic lymphadenectomies, respectively. Additional interventions, such as nephrectomy (3 cases), removal of small bowel sections (7 cases), removal of colon sections (3 cases), and vulvectomy (2 cases), were performed when necessary.

Eight patients (20%) were found to have distant metastasis. Of the patients with a single metastasis, 2 had a metastasis in the abdominal wall and 1 each had a metastasis in the ovary, inguinal lymph nodes, mesentery, and paravaginal tissue. Two patients showed multiple metastases intraoperatively.

The tumors were grade 1 in 4 cases (10%), grade 2 in 14 cases (35%), and grade 3 in 20 cases (50%). In 2 cases (5%), only postirradiation scarring was found without evidence of a tumor. In 29 patients (73%), the tumor entity was an adenocarcinoma.

In 37 patients (92%), a pathological complete removal of the tumor was achieved, and 3 patients (8%) had positive margins. Two of those 3 patients (66%), whom had undergone a primary exenteration, had clear margins. Clear margins were also found in 95% (35/37) of patients who underwent a secondary exenteration.

In 27 cases, no lymph node metastases were found. Two patients were positive for pelvic lymph node metastases and 1 patient was positive for para-aortic lymph node metastases. In addition, 7 patients were positive for both pelvic and para-aortic nodal metastases. Two (29%) of those patients had undergone a primary exenteration (Table 2).

The 30 patients with pathologically free lymph nodes had a 5-year survival rate of 63.3% and a 10-year survival rate of 57.0%.

The overall survival rate was 61.4% at 5 years and 51.1% at 10 years (Fig. 1). For the 31 patients who underwent pelvic exenteration with a curative aim, the overall survival rates were higher than those for the entire study population and were 72.6% at 5 years and 59.4% at 10 years (Fig. 2).

For the 9 patients who underwent a palliative exenteration, the survival rate was 19.1% at 5 years and 0% at 10 years (Fig. 2). Two of those 9 patients died, 1 at 2 months after exenteration because of sepsis and 1 because of general weakness. Three patients died because of distant pulmonary metastasis, and 1 patient died because of new tumor recurrence. Three patients, who were all at least the age of 60 years, were lost to follow-up after 5, 8, and 108 months.

The patients who were at the age of 43 to 55 years (8, 20%) had survival rates of 100% at 5 years and 75% at 10 years. The patients who were at the age of 56 to 64 years (14, 35%) had a survival rate of 61.6% at both 5 and 10 years. The patients older than 65 years (18, 45%) had survival rates of 40.2% at

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**TABLE 2. Lymph node status at initial treatment and exenteration**

<table>
<thead>
<tr>
<th>Pretreatment Form</th>
<th>n</th>
<th>Lymph node status initial treatment</th>
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<th>Pelvic lymphadenectomy</th>
<th>Para-aortic lymphadenectomy</th>
<th>Post pelvic lymph nodes</th>
<th>Post para-aortic lymph nodes</th>
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<td></td>
<td></td>
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<tr>
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<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Performed, missing report</td>
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<td>11</td>
<td>11</td>
<td>3</td>
<td>2</td>
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<td>Tumor-free</td>
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<td></td>
<td></td>
<td>Metastasis</td>
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<tr>
<td>Radiation</td>
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<td>0</td>
<td>2</td>
<td>20</td>
<td>19</td>
<td>4</td>
</tr>
<tr>
<td>Operation and radiation</td>
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<td>Not performed</td>
<td></td>
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<td>Metastasis</td>
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**FIGURE 1.** Overall survival after pelvic exenteration in patients with primary advanced or recurrent endometrial cancer (Kaplan-Meier curve).
5 years and 30.2% at 10 years. The difference in the overall survival rates between the youngest and the oldest cohort was statistically significant ($P = 0.03$, Fig. 3). The 8 patients who were between the age of 43 and 55 years had a survival rate of 100% at 5 years. They all underwent an exenteration with a curative aim; 4 (50%) of the 8 patients underwent a posterior exenteration and the other 4 patients underwent a total exenteration. One patient (1/8, 12.5%) in this age range underwent a primary exenteration and 7 (7/8, 87.5%) underwent a secondary exenteration; all 8 patients had complete resection confirmed microscopically. The tumors were graded G0 (no tumor residual) for 1 patient (1/8, 12.5%), G1 for 1 patient (1/8, 12.5%), G2 for 2 patients (2/8, 25%), and G3 for 4 patients (4/8, 50%). No patient had metastasis in the pelvic lymph nodes. One patient had para-aortic lymph node metastasis, and 2 patients had metastases in the mesenteric lymph nodes.

Considering only the homogenous group of the 15 patients with adenocarcinoma who underwent exenteration with a curative aim and for whom pathological free margins were achieved, no lymph node metastases were present, and no evidence of lymphangiosis was observed, we achieved a survival rate of 77.5% at 5 years and of 64.6% at 10 years.

Complications occurred in 12 (30%) of 40 patients. Seven patients had 1 complication, such as abscess formation, ileus, fistula, lymph cyst, septicemia, thrombosis, etc. Two patients had 2 complications, and 3 patients had more than 2 complications.

In this study, which included many elderly patients, the cause of death was local recurrence for 2 patients and distant metastasis for 5 patients. For 12 patients, the cause of death was not tumor related. At the time of this publication, 2 patients were still living and their lung metastases had been removed. The perioperative mortality rate (30 postoperative days) was 7.5% (3/40).

**DISCUSSION**

The main indication for pelvic exenteration is the central persistence or recurrence of gynecologic cancers. A major issue when comparing published data regarding pelvic exenterations is the heterogeneity of patient groups. In numerous studies, patients with different gynecologic cancers are not analyzed separately; therefore, the results of those studies should be interpreted with caution. The study presented here describes a series of a single gynecologic cancer entity, endometrial cancer, and solely depicts clinical outcome after pelvic exenteration. Although many parameters, such as perioperative morbidity and mortality rates after pelvic exenteration, are similar between different cancer types, there are some interesting distinctions that require closer consideration.

The first reported perioperative mortality rate for pelvic exenteration for primary advanced or recurrent endometrial carcinoma was 23%, and this has decreased to between 0% and 10%. In our study, there were no intraoperative deaths, and the perioperative mortality rate was 7.5%, which is comparable with those reported previously in the literature.

Morbidity rates of up to 75% have been reported by earlier publications. Because of improvement in perioperative care, operative morbidity has noticeably declined for the last few decades. Our complication rate of 30% is within the reported range for pelvic exenteration, although 37 (92%) of our 40 patients were pretreated, and the majority of them (24/37, 65%) were pretreated more than once. Regardless of these pre-treatments, we achieved complete continent reconstruction of the neobladder and colon in 80% (32/40) of our patients. Of the initial 18 patients who underwent a protective colostomy, 8 were resected and 10 were maintained because of patient request.

The 5-year overall survival rate of 40 patients with primary advanced or recurrent endometrial cancer was 61.4%. The best outcome was observed in the youngest age group (43–55 years). All women in that group survived 5 years. For this age group, no advantage was found with regard to negative prognostic features, such as high grading (G3: 4/8, 50%). The oldest patient group (>65 years) had a 5-year survival rate of 40.2% and a 10-year survival rate of 30.2%, which indicates that pelvic exenteration is still a viable option for these patients, with a long-term survival rate. Furthermore, these data are in accordance with those of other authors.

For patients undergoing pelvic exenteration with a curative intent, the survival rate of patients with primary advanced
or recurrent cervical cancer is higher than that of patients with endometrial cancer (72.6% vs 64% at 5 years and 59.4% vs 57% at 10 years).\textsuperscript{18} However, because of the small cohort in this study, this difference was not statistically significant (\(P = 0.70\)).

This difference in survival rate may be due to the different biological behaviors (parametrical vs nodal invasion) of these 2 cancer entities and once again indicates the problem of analyzing outcomes after pelvic exenterations in an inhomogeneous cohort. Another observed difference between endometrial and cervical cancer is the presence of mesorectal lymph node metastasis without infiltration of the rectum. Although mesocolic lymph node metastasis clearly decreases the 5-year overall survival of patients with cervical cancer,\textsuperscript{18} this was not found in patients with endometrial cancer. Of 3 patients with mesocolic lymph node metastasis, 2 patients experienced long-term survival with no other lymph node metastases and 1 patient died after R1 resection shortly after the operation.

When major symptoms, such as pelvic pain, bowel obstruction, and fistula formation, substantially reduce patient quality of life, palliative exenteration may be considered, not only to improve quality of life but also to improve survival. In support of this, the patients in our study who underwent palliative exenteration had a 5-year survival rate of 19.1%. Other therapy options, such as chemotherapy, radiation, and the combination of the two, show overall survival rates of a few months and sometimes cause severe adverse effects. In a phase 2 trial, patients with persistent or recurrent endometrial cancer receiving bevacizumab had a median progression free survival of 4.2 months and an overall survival of 10.5 months.\textsuperscript{19} Several other phase 2 and 3 trials with single agent chemotherapy showed a limited response rate that typically lasted for only several months.\textsuperscript{20} Because of the lack of alternative effective treatment options, pelvic exenteration may be a reasonable alternative.

Although patients with primary advanced endometrial cancer represent only a small portion of patients with newly diagnosed uterine cancers, they have a high percentage of disease-related deaths, with low survival rates in patients with advanced stage or recurrent disease.\textsuperscript{10–24} Women with advanced stage or recurrent disease are often multimorbid, obese, and older than women with other uterine cancers; thus, frequently, they are not considered ideal candidates for extensive surgeries, such as pelvic exenteration, even though studies have shown that mortality can be decreased when surgery is performed.\textsuperscript{6}

The limitations of our study are its retrospective character and relatively small cohort. However, the 40 cases presented here represent the largest patient cohort with advanced or locally recurrent endometrial cancer who underwent pelvic exenteration published to date. Generally, studies describing pelvic exenteration often do not include a control group or a comparison group. Only a few studies have compared pelvic exenteration with radiotherapy, and we did not find any studies that compared exenteration with chemotherapy. The limited data available demonstrate that pelvic exenteration may provide some benefits over radiation, although larger studies are necessary to support this finding.\textsuperscript{25}

Improvements in operative technique have resulted in the more frequent achievement of pathological free margins. There are limited treatment options available for women with advanced or recurrent endometrial cancer, and exenteration is the only treatment that provides the possibility of cure. Our finding of a 5-year overall survival rate of 61.4% supports the findings of other authors, who also showed high survival rates when pathologically free margins are achieved.

**REFERENCES**


