Laparoscopic treatment of endometrial cancer: five-year recurrence and survival rates

J.F. Magrina[1], *M.D.*; **A.L. Weaver**[2], *MS*

[1]*Department of Obstetrics and Gynecology, Mayo Clinic, Scottsdale, AZ;* [2]*Division of Biostatistics, Mayo Clinic, Rochester, MN (USA)*

Summary

Purpose: To evaluate the 5-year recurrence and survival of patients with clinical Stage I endometrial cancer treated by the laparoscopic approach.

Methods: Retrospective review of 56 patients with clinical Stage I endometrial cancer treated laparoscopically. The mean follow-up was 6.4 (4.8-9.6) years. The International Federation of Obstetricians and Gynecologists (FIGO) surgical staging was: I, 45 (80.4%); II, three (5.4%); III, six (10.7%); and IV, two (3.6%).

Results: For patients with surgical Stage I (n = 45), the 5-year recurrence rate was 4.9% and the 5-year cause-specific survival was 94.7%. Factors univariately associated with survival were grade (p = .017), depth of myometrial invasion (p = .018), node metastasis (p = .013), and surgical stage according to FIGO (p = .097).

Conclusion: The laparoscopic approach provided 5-year survival and recurrence rates similar to those previously attained by laparotomy in our institution.

Key words: Endometrial cancer; Hysterectomy; Laparoscopic lymphadenectomy,

Introduction

A preliminary comparison study of endometrial and cervical cancer patients treated by laparotomy versus laparoscopy at the Mayo Clinic revealed major advantages for the laparoscopic group [1]. The perioperative morbidity and 3-year recurrence and survival rates have been reported [2]. A review of the follow-up of these patients with clinical Stage I endometrial cancer was done, and the 5-year survival and recurrence rates are reported here.

Materials and Methods

The records of 56 patients with a diagnosis of clinical Stage I invasive endometrial cancer were reviewed. These patients underwent a hysterectomy (vaginal in 44 and laparoscopic in 6), bilateral salpingo-oophorectomy, and laparoscopic pelvic and/or aortic lymphadenectomy. Patients undergoing a conversion to laparotomy underwent an open abdominal hysterectomy (6 patients).

The patients' records were abstracted for age, type of surgical procedure, type and grade of tumor, depth of myometrial invasion, surgical staging, lymph node involvement, number of lymph nodes retrieved, recurrence, and survival. All patients known to be alive at the time of the review were contacted about the disease status. In all instances of death or recurrence, the pertinent medical records were reviewed. Among the 45 patients currently alive at the last contact, the mean follow-up was 6.4 years (range, 4.8-9.6 years).

Estimates of recurrence, cause-specific survival, and overall survival were made by using the Kaplan-Meier method. Comparisons of survivorship curves among subgroups were made with the log-rank test. All calculated p values were two-sided, and p values less than .05 were considered statistically significant.

Revised manuscript accepted for publication March 15, 2004

Results

Mean patient age was 69.6 years (range, 43-86 years); mean weight, 68.0 kg (range, 47-111 kg). The pathologic and perioperative data, including morbidity, have been reported elsewhere [2]. Adenocarcinoma was noted in 49 patients (87.5%), adenoacanthoma in three (5.4%), adenosquamous carcinoma in two (3.6%), papillary serous carcinoma in one (1.8%), and mixed endometrioid and clear cell carcinoma with sarcomatoid features in one (1.8%). The International Federation of Obstetrics and Gynecology (FIGO) [3] tumor grading was as follows: grade 1, 13 patients (23.2%), grade 2, 27 (48.2%); and grade 3, 16 (28.6%). Myometrial invasion was assigned as follows: no invasion, six patients (10.7%); ≤ 50% invasion, 33 (58.9%); and > 50% invasion, 17 (30.4%). Lymph-vascular space permeation was diagnosed in five patients (8.9%). Involvement of other structures included the cervix in five patients (8.9%), adnexa in three (5.4%), and pelvic peritoneum in three (5.4%). FIGO surgical staging was: I, 45 (80.4%); II, three (5.4%); III, six (10.7%); and IV, two (3.6%).

The mean number of lymph nodes removed was 19.4 (range, 7-39). Lymph node metastases were identified in seven patients (12.5%) and distributed as follows: pelvic, five (8.9%) and aortic, four (7.1%). Two patients (3.6%) had both pelvic and aortic node metastases.

Postoperative pelvic irradiation was administered to 11 patients (19.6%). Combination chemotherapy (4 cycles of methotrexate, doxorubicin, cisplatin, and vinblastine) was administered to one patient with extrauterine metastases.

Recurrences were detected in six patients (Stage IB, one; IC clear cell, one; IIB, one; IIIC, two; IVB, one), three of whom had received pelvic irradiation. There

were no instances of vaginal cuff, vaginal suture line, trocar site, or isolated pelvic recurrences. Recurrences were distant in five patients (2 in the liver, 1 in the lungs, 1 in the abdomen and liver, and 1 in the abdomen, liver and lungs), and in one the recurrence was local and distant (lower posterior vagina and lungs). They all died of their uterine malignancy. For patients with surgical Stage I tumor (n = 45) the 5-year recurrence rate was 4.9% and for clinical Stage I patients it was 11.1%.

An additional 11 patients died during the follow-up period of causes unrelated to their uterine malignancy. The 5-year cause-specific survival rate for patients with surgical Stage I (n = 45) was 94.7% and for clinical Stage I patients (n = 56) it was 88.5%.

The 5-year overall survival rate for clinical Stage I patients was 68.2%. The 5-year overall survival rate for patients with surgical Stage II to IV (n = 11) was 63.6%.

The number of recurrences or deaths due to disease was too small to assess for risk factors. However, five of six patients with recurrence and death from disease had grade 3 tumors and > 50% myometrial invasion. Factors univariately associated with survival were grade (p = .017), depth of myometrial invasion (p = .018), node metastasis (p = .013), and surgical stage according to FIGO (p = .097).

Discussion

There is little doubt that the laparoscopic approach is effective therapy for patients with endometrial carcinoma, is associated with a similar or lower complication rate, and provides shorter hospitalization and earlier recovery compared to the abdominal approach. One can only anticipate that once laparoscopic techniques are widely used by gynecologic oncologists, they will be considered the standard surgical approach for patients with early endometrial carcinoma, whereas the open technique will remain an alternative or be reserved for selected patients with advanced disease or unsuitable for laparoscopy.

In a previous comparison study from Mayo Clinic of patients with early endometrial and cervical cancer, we [1] observed advantages for the laparoscopic group compared with a matched group of patients treated abdominally. Particularly noted were reductions in the operative blood loss, number of blood transfusions, days of urethral catheterization, and hospitalization time. In comparable analyses, other authors have reached similar conclusions [4, 5]. Postoperative complications after laparoscopic treatment are reduced [6, 7] or similar [8, 9], likely related to the laparoscopic expertise of the operating surgeon and the patient's co-morbidities. In a comparison series [6], the morbidity associated with the laparotomy incision was 100 times higher (17%) than that of the laparoscopy group (0.16%).

There is general agreement that operative blood loss, blood transfusions, and number of hospital days are significantly reduced for laparoscopy patients [1, 4-6, 8-10]. Additionally, an earlier return to normal activities [5, 11] and reduced overall hospital costs [5, 7] are associated with the laparoscopic approach.

Our mean follow-up of 6.4 years is adequate to establish a meaningful comparison with recurrence and survival rates of patients previously treated by the abdominal approach at our institution. The local control of the disease in our laparoscopy patients was excellent, as demonstrated by the fact that there were no isolated pelvic recurrences and only one vaginal recurrence (lower third of the posterior vaginal wall) in association with a distant recurrence. All six patients with recurrence had concurrent distant metastases and died of their disease, for a 5-year recurrence rate of 11.1% for patients with clinical Stage I. This rate of recurrence compares favorably with an observed 5-year recurrence rate of 9% (n = 52) among 577 patients with clinical Stage I previously treated at Mayo Clinic [12].

There were only two recurrences among the 45 patients with surgical Stage I, for a 5-year recurrence rate of 4.9%. One of these patients had a grade 3 clear cell tumor with > 50% myometrial penetration, and the other had an adenocarcinoma Stage IB grade 1.

Other authors have observed no pelvic recurrences in patients treated by laparoscopy [8, 9], no difference in recurrence rates [8, 13] or between sites of recurrence among laparoscopy and laparotomy patients [13], and no instances of vaginal cuff recurrence [8, 9, 13], indicating the adequacy of the laparoscopic approach. No trocar site recurrences were noted in a compilation of 519 patients with endometrial cancer from five series, including the present one [6, 8, 9, 13].

The effectiveness of the laparoscopic approach is demonstrated by a 5-year disease-free survival of 94.7% for Stage I patients. Similar results, although with a shorter follow-up, have been observed by other authors (Table 1). Additionally, comparison studies with laparotomy have shown similar disease-free survival rates for both groups of patients (Table 2). In this series, the 5-year cause-specific survival of 88.5% for patients with clinical Stage I was similar to that of patients with clinical Stage IA (89%) and IB (82%) previously treated at our institution by the abdominal approach (14).

Table 1. — *Disease-free survival rates of patients with early endometrial cancer treated by laparoscopy.*

Author	Year	N	Mean FU (mos.)	% DFS
Malur *et al.* [9]	2001	37	16.5	97.3
Holub *et al.* [8]	2002	177	33.6	93.7
Eltabbakh *et al.* [13]	2002	100	27.0	93.0
Present study	2003	45	76.0	94.7

DFS: disease-free survival; FU: follow-up.

Table 2. — *Disease-free survival rates of patients with early endometrial cancer treated by laparoscopy or laparotomy.*

	Laparoscopy			Laparotomy		
Author	N	Mean FU (mos.)	% DFS	N	Mean FU (mos.)	% DFS
Malur *et al.* [9]	37	16.5	97.3	33	21.6	93.3
Holub *et al.* [11]	177	33.6	93.7	44	45.2	93.2
Eltabbakh *et al.* [13]	100	27	93	48	86	90

DFS: disease-free survival; FU: follow-up.

The 5-year overall survival rate for patients with clinical Stage I tumor was 68.2% and compares to 77.7% [12] observed at our institution in a similar group of patients treated by the abdominal approach. The difference between the cause-specific and the overall survival indicates a high-risk population, as demonstrated by 82.1% and 69.6% of the patients having associated co-morbidities and having had previous abdominal operations, respectively [2].

In conclusion, 5-year recurrence and survival rates for patients with endometrial cancer treated by laparoscopy are similar to those of patients treated by laparotomy. At a time when quality-of-life issues are being addressed, the laparoscopic approach should be preferable because it offers major advantages over laparotomy treatment without compromising results.

References

[1] Magrina J.F., Serrano L., Cornella J.L.: "Laparoscopic lymphadenectomy and radical or modified radical vaginal hysterectomy for endometrial and cervical carcinoma: preliminary experience". *J. Gynecol. Surg.*, 1995, *11*, 147.

[2] Magrina J.F., Mutone N.F., Weaver A.L., Magtibay P.M.: "Fowler RS, Cornella JL. Laparoscopic lymphadenectomy and vaginal or laparoscopic hysterectomy with bilateral salpingo-oophorectomy for endometrial cancer: morbidity and survival". *Am. J. Obstet. Gynecol.*, 1999, *181*, 376.

[3] FIGO Cancer Committee: "Staging announcement". *Int. J. Gynecol. Obstet.*, 1989, *28*, 190.

[4] Boike G., Lurain J., Burke J.: "A comparison of laparoscopic management of endometrial cancer with traditional laparotomy" (abstract). *Gynecol. Oncol.*, 1994, *52*, 105.

[5] Spirtos N.M., Schlaerth J.B., Gross G.M., Spirtos T.W., Schlaerth A.C., Ballon S.C.: "Cost and quality-of-life analyses of surgery for early endometrial cancer: laparotomy versus laparoscopy". *Am. J. Obstet. Gynecol.*, 1996, *174*, 1795.

[6] Manolitsas T.P., McCartney A.J.: "Total laparoscopic hysterectomy in the management of endometrial carcinoma". *J. Am. Assoc. Gynecol. Laparosc.*, 2002, *9*, 54.

[7] Gemignani M.L., Curtin J.P., Zelmanovich J., Patel D.A., Venkatraman E., Barakat R.R.: "Laparoscopic-assisted vaginal hysterectomy for endometrial cancer: clinical outcomes and hospital charges". *Gynecol. Oncol.*, 1999, *73*, 5.

[8] Holub Z., Jabor A., Bartos P., Eim J., Urbanek S., Pivovarnikova R.: "Laparoscopic surgery for endometrial cancer: long-term results of a multicentric study". *Eur. J. Gynaecol. Oncol.*, 2002, *23*, 305.

[9] Malur S., Possover M., Michels W., Schneider A.: "Laparoscopic-assisted vaginal versus abdominal surgery in patients with endometrial cancer - a prospective randomized trial". *Gynecol. Oncol.*, 2001, *80*, 239.

[10] Langebrekke A., Istre O., Hallqvist A.C., Hartgill T.W., Onsrud M.: "Comparison of laparoscopy and laparotomy in patients with endometrial cancer". *J. Am. Assoc. Gynecol. Laparosc.*, 2002, *9*, 152.

[11] Holub Z., Voracek J., Shomani A.: "A comparison of laparoscopic surgery with open procedure in endometrial cancer". *Eur. J. Gynaecol. Oncol.*, 1998, *19*, 294.

[12] Malkasian G.D. Jr., Annegers J.F., Fountain K.S.: "Carcinoma of the endometrium: Stage I". *Am. J. Obstet. Gynecol.*, 1980, *136*, 872.

[13] Eltabbakh G.H.: "Analysis of survival after laparoscopy in women with endometrial carcinoma". *Cancer*, 2002, *95*, 1894.

[14] Malkasian G.D. Jr.: "Carcinoma of the endometrium: effect of stage and grade on survival". *Cancer*, 1978, *41*, 996.

Address reprint requests to:
J.F. MAGRINA, M.D.
Department of Obstetrics
and Gynecology
Mayo Clinic
13400 East Shea Boulevard,
Scottsdale, AZ 85259 (USA)