Is Total Laparoscopic Surgery for Endometrial Carcinoma at Risk of Local Recurrence? A Long-term Survival

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Abstract. Background: Loco-regional recurrences after laparotomic surgery for early endometrial carcinoma have an incidence of 3-8%. This study examined the pattern of recurrences and survival after full laparoscopic hysterectomy. Patients and Methods: Between January 1997 and December 2002, 113 consecutive patients with pre-operative Stage I endometrial cancer, self-referred to two different surgical teams, were treated by the laparoscopic approach by one team and by the laparotomic approach by the other team. Results: Nineteen patients were treated by total laparoscopic hysterectomy (TLH) by the endoscopic group, and 94 were treated by total abdominal hysterectomy (TAH) by the oncologic group. Sixteen patients (84.2%) in the laparoscopic group and 79 patients (84.0%) in the laparotomic group had Stage I disease. The mean age and mean weight did not differ in the two groups. With a mean follow-up of 52.2 months for the TLH group and 43.6 months for the TAH group, one recurrence (5.3%) was observed in the former group and 9 recurrences (10.6%) in the latter group. No significative differences were observed for disease-free survival and overall survival. Conclusion: Total laparoscopic hysterectomy does not increase the risk of local recurrence and does not affect survival for patients with early stage endometrial carcinoma.

Endometrial cancer is the most common gynaecologic malignancy. Treatment of early stage endometrial carcinoma is primary surgery, traditionally performed by open technique. Peritoneal washing is taken for cytology, a thorough exploratory laparotomy is performed, followed by total abdominal hysterectomy (TAH) and bilateral salpingo-oophorectomy (BSO). Pelvic lymphadenectomy is reserved for women with high-risk factors such as deep myometrial invasion, Grade 3 lesions, large tumors, non-endometrioid histology, or cervical extension of the tumor (1-3). Localregional relapse rates of 3-8%, occur mainly in the vaginal vault and, rarely, on the antero-posterior walls. Distal failures are observed in 6-10% of the patients (1, 2). Relapses are generally associated with high-risk factors; in patients over 60 years old, in those with Grade 2 tumors with outer half of myometrial invasion, and in patients with Grade 3 tumors locoregional relapses rate 10-12% (1).

Laparoscopic surgery is becoming a widespread technique for the treatment of early endometrial carcinoma, as shown by 155 published references obtained from a research of the literature on PubMed. The majority of reported series is about laparoscopic-assisted vaginal hysterectomy. Locoregional relapses for clinical Stage I disease after laparoscopic-assisted vaginal hysterectomy are 2.5-2.7%, corresponding to the results obtained after the open technique (4-7).

We started a two team prospective study to evaluate the relapse rate and overall survival of patients who underwent total laparoscopic hysterectomy (TLH) and pelvic lymphadenectomy with patients who had total abdominal hysterectomy (TAH) and pelvic lymphadenectomy for early endometrial carcinoma.

Patients and Methods

Patients. From January 1997 to December 2002, all patients with diagnosis of early endometrial carcinoma were treated by two surgical teams using different approaches; the team of the Service
of Reproductive Surgery submitted all patients to laparoscopic surgery, while the Department of Gynecology and Obstetrics team treated all patients by a laparotomic approach. The patients were allocated to either the laparoscopic team or laparotomic team at referral. Patients submitted to vaginal hysterectomy for poor medical conditions were excluded from this series. Patients with pre-operative clinical or histological evidence of cervical involvement by tumor, patients who were suspected of having extraterine tumor spread based on clinical, sonographic and magnetic resonance pre-operative work-up, patients treated with primary radiotherapy and patients with no available follow-up information were excluded from this series. The analysis was based on the data of 113 patients. Staging and grading were determined according to the 1988 FIGO criteria (8). General information was collected including age, past medical history, anesthesiologic risk and body mass index (BMI).

Table I. Patients’ profile characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Laparoscopic patients</th>
<th>Laparotomic patients</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>n.</td>
<td>19</td>
<td>94</td>
<td></td>
</tr>
<tr>
<td>Age (years) mean (SD)</td>
<td>61 (10.1)</td>
<td>62 (11.3)</td>
<td>0.721</td>
</tr>
<tr>
<td>Weight(BMI)mean(SD)</td>
<td>27.0 (5.59)</td>
<td>26.4 (3.9)</td>
<td>0.573</td>
</tr>
<tr>
<td>Hystology (n, (%))</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endometrioid</td>
<td>18 (94.7%)</td>
<td>90 (95.7%)</td>
<td></td>
</tr>
<tr>
<td>Serous papillary</td>
<td>1 (5.3%)</td>
<td>4 (4.3%)</td>
<td>0.677</td>
</tr>
<tr>
<td>Myometrial invasion (n, (%))</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No invasion</td>
<td>2 (10.5%)</td>
<td>14 (14.9%)</td>
<td></td>
</tr>
<tr>
<td>&lt;50%</td>
<td>7 (36.8%)</td>
<td>53 (56.4%)</td>
<td></td>
</tr>
<tr>
<td>&gt;50%</td>
<td>10 (52.7%)</td>
<td>27 (28.7%)</td>
<td>0.128</td>
</tr>
<tr>
<td>Grading (n, (%))</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G1</td>
<td>11(61.2%)</td>
<td>63 (70.0%)</td>
<td></td>
</tr>
<tr>
<td>G2</td>
<td>6 (33.3%)</td>
<td>16 (17.7%)</td>
<td></td>
</tr>
<tr>
<td>G3</td>
<td>1 (5.5%)</td>
<td>11 (12.3%)</td>
<td>0.279</td>
</tr>
<tr>
<td>FIGO Staging (n, (%))</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>16 (84.2%)</td>
<td>79 (84.0%)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>0</td>
<td>9 (9.6%)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>3 (15.8%)</td>
<td>6 (6.4%)</td>
<td>0.167</td>
</tr>
<tr>
<td>Lymph node status (n, (%))</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nx</td>
<td>3 (15.8%)</td>
<td>57 (60.6%)</td>
<td></td>
</tr>
<tr>
<td>N0</td>
<td>13 (68.4%)</td>
<td>35 (37.2%)</td>
<td></td>
</tr>
<tr>
<td>N1</td>
<td>3 (15.8%)</td>
<td>2 (2.2%)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

* Chi-square tests.

Table II. Perioperative data.

<table>
<thead>
<tr>
<th></th>
<th>Laparoscopic patients</th>
<th>Laparotomic patients</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>n.</td>
<td>19</td>
<td>94</td>
<td></td>
</tr>
<tr>
<td>Pelvic lymphadenectomy</td>
<td>16</td>
<td>37</td>
<td>0.0001</td>
</tr>
<tr>
<td>Lymph nodes retrieved (n.) mean (SD)</td>
<td>15 (4.0)</td>
<td>20 (11)</td>
<td>0.060</td>
</tr>
<tr>
<td>Duration of hospital stay (days) mean (SD)</td>
<td>7.8 (6.5)</td>
<td>7 (5.9)</td>
<td>0.597</td>
</tr>
</tbody>
</table>

*Chi-square tests.

disease; all patients with Grade 3 disease; and for some patients with Stage III disease. Vaginal cuff brachytherapy was prescribed for patients with Stage IB Grade 2. Patients with multiple (>3 lymph nodes) pelvic lymph nodal metastases and extrapelvic lymph nodal metastases received post-operative chemotherapy and whole abdominal radiation therapy.

In patients treated with laparotomy, a classic extravesical total hysterectomy was performed with 1-2 cm of vaginal cuff resection and bilateral salpingo-oophorectomy. Laterally to the uterus two clamps were positioned across the round ligament and fallopian tubes to gain traction and fallopian tubes obstruction.

Patients allocated to laparoscopy were placed in the lithotomy and deep Trendelenburg position with legs open at 60°. Prior to laparoscopy, a uterine manipulator was placed transvaginally into the endometrial cavity; the manipulator presents a flat obturator to avoid cervical damage and a curved plastic tube displays vaginal fornices and the uterine vessels. Care was taken not to perforate the uterus during insertion of the manipulator. Prior to any uterine manipulation, bipolar coagulation of the fallopian tubes was carried out to avoid tumor cells diffusion into the peritoneal cavity. Bipolar coagulation was used to secure ovarian and uterine vessels. While the pneumoperitoneum was maintained by the tube and a sponge placed in the vagina, a circular colpopotomy was carried out laparoscopically under the guidance of the manipulator’s tube with the monopolar electrode hook. The uterus was removed vaginally. Finally the vaginal vault was sutured either vaginally or by endoscopic intracorporeal suture. Lymph nodes were removed through the trocar using a surgical bag (Endo-catch, Tyco Healthcare Group LP, Norwalk, Connecticut, USA).

Laparoconversion was defined as the substitution of laparoscopy by laparotomy for intra-operative complications. Variables evaluated in post-operative outcome were hemoglobin loss and febrile morbidity (indicated by a temperature of 38°C or higher in two consecutive measurements at least 6 hours apart, excluding the first 24 hours). The length of hospital stay, in term of hours of hospitalization after surgery, was noted. Before hospital discharge, patients had to tolerate a normal diet, be able to dress themselves, be fully mobile around the ward, be analgesic-free and satisfied that they could manage at home.

Oncologic details were recorded, including histological type, grading, myometrial invasion, and tumor stage on the surgical specimen. The positivity of peritoneal washing, number and
positivity of collected lymph nodes were recorded. Post-operative radiotherapy and chemotherapy were reported. A history was obtained and pelvic examination was done at a 4- month interval; patients received a pelvic ultrasound twice a year; a pap-smear of the vaginal vault, a chest radiogram and a hepatic scan were requested once a year. The type of recurrence, subsequent treatment and survival were recorded.

Statistical analysis. A comparison of age and body weight was performed using the t-test, and Chi-square tests were used to compare the distribution of frequencies. Disease-free survival (DSF) was defined as the period from surgery until the date of first recurrence. Overall survival (OS) was defined as the time from surgery to death. Data on patients who were alive were censored at the last follow-up visit. Univariate analysis of DFS and OS was performed with the Kaplan-Meier method and survival curves were compared using the log-rank test. P values are the result of two-sided tests and \( p < 0.05 \) was considered to indicate a statistically significant difference. All statistical analyses were carried out with STATA for Windows® (STATA Corporation, College Station, TX, USA).

Results

The results are summarized in Tables I and II. One hundred and thirteen patients were analyzed; 19 patients received TLH and 94 patients received TAH. The median age was similar in the two groups; 62 years (range 37-88) in the laparoscopic group, 61 years (range 43-76) in the laparotomic group. The difference in the body mass index between groups was not substantial; mean 26.4 in the laparoscopic group compared to 27.0 in the laparotomy group. Among the laparoscopic patients, no case requested a conversion to laparotomy.

Major post-operative complications (intrabdominal bleeding, bowel occlusion, pelvic abscess, major abdominal evisceration) were absent, apart from a case of urinary fistula which occurred in the laparoscopic group; endoscopic positioning of a double J uretheral stent and 10 days’ recovery were needed. The mean post-operative stay was 6.3 days and 8.3 days in the laparoscopic and laparotomic groups, respectively (\( p = 0.597 \)).

Lymph node dissection was performed in 16 patients (84.2%) in the laparoscopic group and in 37 patients (39.4%) in the laparotomic group. The number of lymph node dissections was not statistically different between the two groups (\( p = 0.037 \)).

Table III. Adjuvant therapy and survival.

<table>
<thead>
<tr>
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<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>n.</td>
<td>19</td>
<td>94</td>
<td></td>
</tr>
<tr>
<td>Adjuvant radiotherapy (n)</td>
<td>9</td>
<td>20</td>
<td>0.037</td>
</tr>
<tr>
<td>Adjuvant chemotherapy (n)</td>
<td>0</td>
<td>1</td>
<td>0.373</td>
</tr>
<tr>
<td>No adjuvant therapy (n)</td>
<td>10</td>
<td>74</td>
<td>0.037</td>
</tr>
<tr>
<td>Mean follow-up (months)(SD)</td>
<td>52.2 (44.5)</td>
<td>43.6 (59.4)</td>
<td></td>
</tr>
<tr>
<td>Recurrences (n.)</td>
<td>1</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Disease-free (n.)</td>
<td>18</td>
<td>85</td>
<td>0.693</td>
</tr>
<tr>
<td>Recurrence-related death (n.)</td>
<td>1</td>
<td>1</td>
<td>0.999</td>
</tr>
</tbody>
</table>

*Chi-square tests.
nodes retrieved was similar in the two groups (a mean of 15 and 19 lymph nodes in the laparoscopic and laparotomic groups, respectively).

Endometrioid adenocarcinoma was the most common histology found in both groups (95.7% and 94.7% in the laparoscopic and laparotomic groups, respectively). No myometrial invasion or less than half of myometrial depth invasion were seen in 67 (71.3%) and 9 (47.3%) cases in the laparotomic and laparoscopic groups, respectively. The difference did not reach statistical significance.

Low-risk stage I endometrial cancer (grade 1-2 endometrioid type with less than halfway myometrial invasion) was seen in 52 (55.3%) and 8 (42.1%) in the laparoscopic and laparotomic groups, respectively. Three cases in the laparoscopic group and 6 cases in the laparotomic group presented at histology a Stage III carcinoma; in the TLH group, all 3 patients were classified as Stage III because of lymph node metastasis; in the TAH group, the 6 patients presented lymph node metastasis in 2 cases, ovarian tumor spread in 3 cases, and positive pelvic cytology in 1 case.

Adjuvant radio- or chemotherapy was administered in 9 patients (47.4%) in the endoscopic group and in 21 patients (22.3%) in the open surgery group.

A mean follow-up of 52.2 and 43.6 months in the two groups showed 9 recurrences in the laparoscopic group (9.6%) and 1 recurrence in the laparotomic group (5.3%). In the laparotomic group, 7 out of 9 recurrences were local (5 vagina, 1 parametrium, 1 bladder), and 2 were distal recurrences (1 bone, 1 axillary lymph nodes). All were loco-regional recurrences. They were treated with salvage radiotherapy in 7 cases and surgery in 2 cases. In the laparoscopic group, a central pelvic relapse in a Stage III patient was detected 4 months post-surgery. The patient was affected by a Grade 2 neoplasia with outer half of the myometrium invasion, lymph vascular space involvement, and two lymph node metastases. No port-site metastasis was observed in the series.

Two patients died of the disease, 1 in the laparoscopic group (5.3%) and 1 (1.1%) in the laparotomic group. Disease-free survival and overall survival did not differ significantly for both groups (Table III and Figures 1 and 2).

Discussion

The surgical treatment for early stage endometrial cancer is highly variable and is currently under investigation; the classic standard treatment is total abdominal hysterectomy and bilateral salpingo-oophorectomy, with pelvic and/or paraaortic lymph node dissection if risk factors are present (1, 2). In recent years, many reports have been dedicated to the use of laparoscopic-assisted vaginal hysterectomy for the treatment of this neoplasia (3-7, 9-11); the procedure associates a laparoscopic salpingo-oophorectomy and lymphadenectomy to vaginal removal of the uterus. The procedure does not seem to modify the incidence of recurrences or the overall survival (4-7). Recently, surgeons have started to perform hysterectomy using a totally laparoscopic approach; the procedure has some advantages over the laparoscopy-assisted procedure; it avoids the time loss necessary to shift from the laparoscopic approach to the vaginal one, and vice versa, after the completion of the vaginal hysterectomy; it permits the choice intra-abdominally under direct visualization of the site for the vaginal cuff resection; and, last but not least, it permits an easy removal of the uterus and adnexa, even in a fixed position.
uterus and with a narrow vagina. The application of the
procedure in oncology should give the same result as the
standard treatment concerning correct removal of the
neoplasia and, subsequently, relapse rate. We analyzed the
long-term incidence of pelvic recurrences in a group of
patients submitted to full laparoscopic hysterectomy for
early endometrial carcinoma.

Pelvic recurrences of endometrial carcinoma are
generally observed as nodules on the vaginal cuff or areas
of thickness on the vaginal walls, or nodules fixed to the
pelvic wall; in early stages neoplasia, the incidence of these
relapses is 4-15% according to a recent analysis of 714
patients of the PORTEC trial (1). To reduce the risk of
antegrade and retrograde tumor seeding during laparotomic
and vaginal hysterectomies, various techniques have been
suggested, such as minimal manipulation of the uterus and
pre-operative occlusion of the fallopian tubes (12), pre-
operative suture of the cervix (13) and Teflon cervical
obturators (14). Schneider suggested pre-operative vaginal
cleansing of the vagina with physiological saline and 96%
ethanol alcohol (15). Recently, Chu et al. reported three cases
of vaginal cuff recurrences for early endometrial carcinoma
controlled by laparoscopic-assisted vaginal hysterectomy (16),
raising concern about the excessive manipulation of the
uterus with this technique. The data are not confirmed by
various other published reports, presenting similar
recurrence rates in patients submitted to laparoscopic-
assisted hysterectomy and laparotomic hysterectomy (4, 6,
7) (Table III). Indeed, manipulation of the uterus during
laparoscopic-assisted hysterectomy is not inherent in the
technique, as the insertion of an endouterine manipulator
is unnecessary and the bipolar coagulation of the fallopian
tubes can easily be carried out laparoscopically (17, 18).

Fully laparoscopic hysterectomy requires the insertion in
the cervical canal of the manipulator; the anterior, posterior
and lateral aspect of the uterus are visualized by the
operator through the push-up offered by the second
assistant seated between the legs of the patients. A 1-cm
vaginal cuff removal is easily obtained, as the operator
recognizes on the manipulator cuff the limit of the cervix
and can tailor the incision of the anterior and posterior
vaginal wall (19). The expected higher incidence of loco-
regional relapses has not been observed by some series (5,
20) (Table II). Magrina et al. reported a series of 56 patients
treated by laparoscopic lymphadenectomy and vaginal (44
patients) or laparoscopic hysterectomy (6 patients) with one
isolated vaginal recurrence in the lower posterior vaginal
wall at 2.4 years of follow-up (5). Obermaier et al., in a
retrospective review of 510 patients submitted to total
laparoscopic surgery or laparotomic surgery, observed at
29-month follow-up a loco-regional relapse of 0.4% in the
first group and of 6.4% in the latter; after adjustment for
age, stage, grade of differentiation, depth of myometrial
invasion and histological type, the two groups demonstrated
similar patterns of recurrence and similar probabilities for
overall survival (20). In the present study of 113 patients
with longer follow-up (45 months), we compared the pattern
of recurrence and survival after total laparoscopic surgery
or laparotomic surgery for early endometrial carcinoma; one
patient presented a pelvic recurrence in the laparoscopic
group (5.3%) and 7 patients presented isolated pelvic
recurrences in the laparotomic group (7.4%). The two
surgical techniques presented similar disease-free survival
and overall survival.

Port-site recurrences after laparoscopic-assisted
hysterectomy have been reported (21, 22), but large series
have not confirmed these preliminary data (4-7). Major
uterine manipulation during total laparoscopic hysterectomy
can theoretically cause a risk of port-sites neoplastic
seeding; Obermaier et al., who used transvaginal removal of
lymph nodes and did not specify fallopian occlusion, in his
series of 226 total laparoscopic hysterectomies, observed no
port-site recurrence; in this series, lymph nodes were
removed with a surgical endo-bag and fallopian tube
occlusion was routinely performed before hysterectomy
(20). The data confirm the absence of port-site metastasis
after total laparoscopic surgery when a precise technique is
employed.

This study followed the patients submitted to total
laparoscopic surgery or laparotomic surgery for early
endometrial carcinoma for a mean of 45 months and
represents the longest follow-up published on this issue
(Table IV). This follow-up represents a period of time
sufficiently long to evaluate the relapses of endometrial
carcinoma, as the median time to relapse, as shown by the
PORTEC trial, is 21 months, with 75% of relapses
diagnosed within 3 years (1). Our data confirm previous
series, suggesting that an influence of the surgical approach
on loco-regional relapses is unlikely.

The role of post-operative radiotherapy is still debated,
but it certainly lowers the loco-regional relapse rate without
modifying the survival rate, as shown by Creutzberg et al.
(1). Our patients were submitted to radiotherapy according
to specific risk factors (Grading 2 and 3, invasion of the
outer half of the myometrium). These risk factors were
present more frequently in the laparoscopic group, and this
is responsible for the higher incidence of post-operative
radiotherapy (47.4%) in the laparoscopic group versus
21.3% in the laparotomic group. The study was conducted
on a series of patients consecutively referred to the two
surgical units and, therefore, the risk factors were not
accurately balanced; certainly the higher incidence of
patients at risk of local recurrence in the laparoscopic group
suggests the adequacy of the surgical procedure.

The search for new procedures with less morbidity,
reduction of hospital charges and higher comfort for the
patients has highlighted, in recent years, laparoscopic-assisted vaginal hysterectomy as a valuable treatment for endometrial cancer (10). The next step is fully laparoscopic hysterectomy and, after the next feasibility of the procedure as reported by Manolititas and McCartney of 161 patients successfully completed in 95% of cases, our study suggests that no higher risk or loco-regional recurrence is associated with the procedure (23). Undoubtedly, our series cannot exclude selection bias, even though the patients were simply allocated into the two groups by self-referral to one of the two surgical units. However, the series was not large enough to draw clear-cut conclusions, and more numerous prospective studies should confirm these preliminary data.

References


7 Eltabbakh GH: Analysis of survival after laparoscopy in women with endometrial carcinoma. Cancer 95(9): 1894-901, 2002.

