High-grade endometrial carcinoma limited to the endometrium or a polyp: is adjuvant treatment necessary?

Leonie Dallaire Nantel, Marie-Claude Renaud, Jean Gregoire, Alexandra Sebastianelli, Marie Plante

HIGHLIGHTS
- Our data indicate no benefit of adjuvant treatment on outcome for patients with serous intraepithelial carcinoma.
- Recurrence rate is low without adjuvant treatment (12%).
- Outcome following treatment for patients with recurrent serous intraepithelial carcinoma is excellent.

ABSTRACT
Objective High-grade endometrial carcinoma limited to the endometrium or a polyp is a rare clinical entity. Currently there is no consensus on standard treatment. Thus, the goal of this study was to evaluate the clinical outcomes of patients with type II endometrial carcinoma without myometrial infiltration or limited to a polyp.

Methods We retrospectively identified type II endometrial carcinoma (FIGO endometrioid grade 3, serous, clear cell, mixed and carcinosarcoma) with spread limited to the endometrium or a polyp from April 2013 to November 2017. Medical records were reviewed for the following information: age at diagnosis, patient characteristics, type of surgery, histology, stage according to FIGO 2009 classification, adjuvant treatments, and site of recurrence. Descriptive statistics and the Kaplan–Meier estimate were used for analysis.

Results A total of 25 patients with a type II stage IA adenocarcinoma were included. All were surgically staged with total hysterectomy, salpingo-oophorectomy, and lymph nodes assessment. The median age at diagnosis was 69 years. All patients had either disease limited to the endometrium (60%) or a polyp (40%). Only four patients had lymphovascular space invasion (16%). The median follow-up was 44 (range 2–67) months. Six patients (24%) received vault brachytherapy only and all others received no adjuvant treatment after surgery (n=19, 76%). Three patients (12%) experienced recurrences at 15, 21, and 55 months after surgery. Following systemic treatment all are alive and disease-free. The 3-year progression-free survival and overall survival were 91% and 100%, respectively.

Conclusion Expectant management with surveillance alone following surgery appears to be safe for patients with high-grade endometrial carcinoma limited to a polyp or the endometrium without myometrial invasion.

INTRODUCTION
Endometrial carcinoma is the most common gynecologic malignancy and the fourth most common cancer diagnosed in women. In 2020, 7400 new cases of endometrial cancer have been diagnosed in Canada and 1300 have died of the disease. Mortality caused by endometrial cancer has increased three-fold over the last few decades. One of the hypotheses explaining this increase in mortality is the increasing incidence of high-grade (type II) endometrial carcinoma. Type II endometrial carcinoma accounts for approximately 20% of all endometrial carcinoma but is responsible for approximately 40% of endometrial cancer deaths. Type II subtypes include uterine serous carcinoma, grade 3 endometrioid, clear cell, carcinosarcoma, and mixed histology. The most common subtype is serous carcinoma which accounts for 11.4% of all endometrial carcinoma, and more than half of all high-grade endometrial carcinoma.

It has been proposed that serous intraepithelial carcinoma is a precursor of uterine serous carcinoma. Both have an identical P53 mutation profile and can be associated with extraterine disease, suggesting that serous intraepithelial carcinoma may be considered as an early form of uterine serous carcinoma rather than a precursor. Histologically, serous intraepithelial carcinoma have no myometrial invasion, typically develop on an atrophic endometrium or polyp, and are characterized by high-grade cellular atypia, polymorphism, and detachment of cells. Although it does not infiltrate the myometrium, it is still associated with extraterine disease in 33%–67% of cases.

Other type II endometrial carcinoma include carcinosarcoma (4.1%), clear cell (3.5%), mixed (4.5%), and grade 3 endometrioid (9.7%). Those types of endometrial carcinoma are also considered high-risk and are treated similar to uterine serous carcinoma. Compared with low-grade endometrioid carcinoma, type II endometrial carcinoma have a higher propensity for lymphovascular space invasion, intra-peritoneal spread, and early distant metastasis. At the time of diagnosis about 60%–70% of patients will have disease outside the uterus.
Original research

The optimal management of early-stage type II endometrial carcinoma is based on histology and recurrence risk, but there is currently no standard treatment for stage IA without myometrial invasion or limited to a polyp. A recent update of the European Society of Gynecological Oncology/European Society for Radiotherapy and Oncology/European Society of Pathology (ESGO/ESTRO/ESP) guidelines for the management of endometrial carcinoma suggested that high-grade endometrial carcinoma limited to a polyp or the endometrium should be classified as intermediate-risk of recurrence. Thus, there is no recommendation for brachytherapy as adjuvant treatment except if other risk factors, such as lymphovascular space invasion, are present. There have been a few retrospective studies with a limited number of patients studying those precise cases. At our center, most patients do not receive adjuvant treatment after surgery. Thus, the goal of this study was to describe the characteristics of our patients with a type II endometrial carcinoma without myometrial infiltration or limited to a polyp. The secondary objective was to evaluate the clinical outcomes of patients observed after surgery (not receiving systemic adjuvant treatment) and compare these to the existing literature.

METHODS

Patient Eligibility
We retrospectively reviewed electronic files of patients who underwent surgery for endometrial carcinoma from April 2013 to November 2017 at our center. This project received approval from our research ethics committee. In accordance with the journal’s guidelines, we will provide our data for the reproducibility of this study in other centers if such is requested. Medical records were reviewed for the following information: age at diagnosis, patient demographics, type of surgery, histology, stage according to International Federation of Gynecology and Obstetrics (FIGO) 2009 classification, adjuvant treatments, and site of recurrence, if any. Only patients with high-grade histology (FIGO endometrioid grade 3, serous, clear cell, mixed, carcinosarcoma) without myometrial invasion or limited to a polyp were included. Patients with or without lymphovascular space invasion were included.

The initial diagnosis for all patients was made by office endometrial biopsy or dilatation and curettage. All surgical approaches were included (laparotomy or minimally invasive surgery). The surgery had to include at least a total hysterectomy with bilateral salpingo-oophorectomy, peritoneal washings, and sentinel lymph node (SLN) mapping, with or without pelvic and para-aortic lymphadenectomy, and omental biopsy. Statistical analysis included Kaplan–Meier estimates for 3-year pelvic progression-free survival and overall survival. Time-to-event was calculated from date of surgical staging.

Studies Inclusion
A literature review was undertaken to identify studies that reported outcomes of patients with stage IA serous endometrial carcinoma limited to the endometrium or a polyp. The literature search was conducted through PubMed. Our research query included “endometrial serous intraepithelial carcinoma”, “serous uterine carcinoma PLUS polyp”, and “serous endometrial carcinoma PLUS endometrium”. Titles and abstracts were reviewed and we identified eight retrospective studies that compared adjuvant treatments and recurrence rates. No prospective studies were identified.

RESULTS

Patient Characteristics
Our retrospective cohort included 856 patients who underwent surgery for endometrial carcinoma. A total of 25 patients (2.9%) had a type II stage IA adenocarcinoma without myometrial invasion in 15 (60%) or limited to a polyp in 10 (40%). Fifteen patients (60%) had a diagnosis of serous intraepithelial carcinoma, 4 patients (16%) had mixed carcinoma with a high-grade component, 2 patients (8%) had clear cell, 3 patients (12%) had grade III endometrioid, and 1 patient (4%) had carcinosarcoma (Table 1). All patients had residual polyp or intraepithelial lesion on the final hysterectomy specimen. Only 4 (16%) patients had lymphovascular space invasion. The mean age at diagnosis was 69 (range 52–91) years. Median body mass index (BMI) was 30 kg/m², and 12 patients (48%) had a BMI below 30 kg/m².

All patients had pre-operative imaging studies. Up to 48% (n=12) of patients had a computed tomography scan of the abdomen and pelvis, 12 (48%) patients had an ultrasound of the abdomen and pelvis, and a pre-operative imaging study was not found for 1 patient (4%). Endometrial thickness was available in 18 patients (62.2%), and the mean thickness was 14 (range 5–30) mm. Pre-operative biopsy showed high-grade neoplasia in 18 (72%) patients, endometrial intraepithelial neoplasia in 4 (16%) patients, and endometrioid carcinoma grade 1 in 3 (12%) patients (Table 1).

Pre-operative CA-125 testing was also available for all patients. The median was 24 (range 5–326) units/mL. The patient with the elevated CA-125 level of 326 units/mL had a concomitant diagnosis of Child C cirrhosis with ascites. Otherwise, all values ranged from 5 to 44 units/mL.

In terms of surgical approach, 12 patients (48%) had robotic surgery, 10 patients (40%) had laparoscopic surgeries, and 3 patients (12%) underwent laparotomy (Table 1). All patients underwent total hysterectomy, bilateral salpingo-oophorectomy, peritoneal washings, and 4 (16%) patients had omental sampling. As for lymph node evaluation, 3 (12%) patients had SLN only (all three had endometrial intraepithelial neoplasia on pre-operative biopsy), 19 (76%) patients had SLN and pelvic node dissection, and 3 (12%) patients had SLN with pelvic and para-aortic lymph node evaluation. Of the 25 patients in which SLN mapping was attempted, 23 (92%) patients had bilateral detection, and 2 (8%) patients had unilateral detection. For those two patients, complete lymph node dissection was performed, either unilateral or bilateral. All patients had negative surgical staging on final pathology.

Adjuvant Treatments
After surgery, most patients did not receive any adjuvant treatments (n=19 or 76%). Of the six patients (24%) who received vaginal vault brachytherapy only, two had presence of lymphovascular space invasion on final pathology. All cases were discussed at our multidisciplinary tumor board. The most frequent reasons for brachytherapy treatment recommendation were grade 3 endometrioid carcinoma (2/3 patients) and clear cell histology (1/2 patients). In addition, 2/4 patients with lymphovascular space invasion received vault brachytherapy.

Recurrences
At the time of the analysis, a total of 3 (12%) patients had recurrences (Online Supplemental Material 1). Two patients died of causes unrelated to endometrial carcinoma. The first patient died...
2 months after surgery from complications of Child C cirrhosis, a condition for which she was awaiting hepatic transplant. The second patient died 4 years after initial surgery from a cause unknown at the time of analysis, but she had no evidence of cancer recurrence at her last follow-up. The median follow-up was 44 (range 2–75) months. Two of 25 patients who recurred had not received adjuvant treatment after their initial surgery and one patient had received vault brachytherapy. Table 2 summarizes those three cases.

The 3-year progression-free survival and overall survival were 91% and 100%, respectively (Figure 1A,B).

**Table 1** Patients (n = 25) and tumor characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age at diagnosis (years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>69</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>55–91</td>
<td></td>
</tr>
<tr>
<td><strong>BMI (median) (kg/m2)</strong></td>
<td>30</td>
<td></td>
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<tr>
<td>&lt;30</td>
<td>12</td>
<td>48</td>
</tr>
<tr>
<td>30–40</td>
<td>9</td>
<td>36</td>
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<tr>
<td>&gt;40</td>
<td>4</td>
<td>16</td>
</tr>
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<td><strong>Pre-operative imaging studies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT scan of abdomen and pelvis</td>
<td>12</td>
<td>48</td>
</tr>
<tr>
<td>Ultrasound of abdomen and pelvis</td>
<td>12</td>
<td>48</td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td><strong>Histology (on pre-operative endometrial biopsy)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-grade carcinoma</td>
<td>18</td>
<td>72</td>
</tr>
<tr>
<td>Endometrioid grade 1</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>Endometrial Intraepithelial neoplasia</td>
<td>4</td>
<td>16</td>
</tr>
<tr>
<td><strong>Histology (on final pathology)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serous</td>
<td>15</td>
<td>60</td>
</tr>
<tr>
<td>Mixed</td>
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<td>16</td>
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<td>Grade 3 endometrioid</td>
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<tr>
<td>Clear cell</td>
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<td>8</td>
</tr>
<tr>
<td>Carcinosarcoma</td>
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<td>4</td>
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<tr>
<td><strong>Polyt</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>10</td>
<td>40</td>
</tr>
<tr>
<td>No</td>
<td>15</td>
<td>60</td>
</tr>
<tr>
<td><strong>Lymphovascular space invasion</strong></td>
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<td></td>
</tr>
<tr>
<td>Yes</td>
<td>4</td>
<td>16</td>
</tr>
<tr>
<td>No</td>
<td>21</td>
<td>84</td>
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<td><strong>CA-125 (units/mL)</strong></td>
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<tr>
<td>Median</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>5–326</td>
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<td><strong>Surgical approach</strong></td>
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<tr>
<td>Robotic surgery</td>
<td>12</td>
<td>48</td>
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<tr>
<td>Laparoscopic surgery</td>
<td>10</td>
<td>40</td>
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<tr>
<td>Laparotomy</td>
<td>3</td>
<td>12</td>
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<td><strong>Surgical staging</strong></td>
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<td></td>
</tr>
<tr>
<td>SLN + pelvic lymphadnectomy</td>
<td>19</td>
<td>76</td>
</tr>
<tr>
<td>SLN + pelvic and para-aortic lymphadnectomy</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>SLN only</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>Omentectomy</td>
<td>4</td>
<td>16</td>
</tr>
<tr>
<td><strong>Follow-up (months)</strong></td>
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<tr>
<td>Median</td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>2–67</td>
<td></td>
</tr>
</tbody>
</table>

BMI, body mass index; CT, computed tomography; SLN, sentinel lymph node.

**DISCUSSION**

**Summary of Main Results**

In our study, the recurrence rate was 12% and all patients were alive and free of disease following salvage systemic chemotherapy treatment. The type of surgical staging did not appear to have an impact on recurrence. However, two of the three patients experiencing recurrence had lymphovascular space invasion on their final pathology report, and one had not received adjuvant brachytherapy.

**Results in the Context of Published Literature**

Our data are similar to older series in the literature (Table 3). A retrospective study published by Chang-Halpenny et al in 2013, showed a similar recurrence rate of 7.8% at 5 years. Most patients in that study did not receive adjuvant treatment (80%), a percentage comparable to our cohort.8 Another study by Liang et al showed a lower recurrence rate (5.9%) at 3 years. Unlike our study, most patients did receive adjuvant treatment (76.5%), but there was no difference in the rate of recurrence whether patients received adjuvant treatment or not.9 Lastly, a recent Canadian study showed a recurrence rate of 12.2% and a 5-year overall survival of 80.7%.11 This cohort is very similar to ours as most patients did not receive any adjuvant treatment. In their retrospective study, the authors also demonstrated that recurrence rates were rare in the omentum and para-aortic area despite the low rate of para-aortic lymphadenectomy (0%) and omental biopsy (51%).

A large retrospective series from the National Cancer Database in the United States was recently published, and unlike our cohort, the 5-year overall survival was 9.4% higher in the chemoradiation group compared with the observation group (81.9% in the observation group compared with 91.3% in the chemoradiation group, p=0.001). Although it is a large cohort, it should be noted that cause of death and cancer-specific progression-free survival were not available, since the information could not be retrieved from the database. Also, more patients in the observation group had government insurance (compared with private insurance) which could explain the difference in overall survival.10

With regards to lymph node staging, a recent expert review has concluded that SLN evaluation is adequate for the staging of...
uterine serous carcinoma. Indeed, the review confirms that accumulating data support the safety and effectiveness of SLN mapping for apparent early-stage uterine serous carcinoma. A series published in 2017 compared survival of patients with SLN mapping versus complete lymphadenectomy and showed no difference in survival, suggesting that SLN alone does not appear to compromise prognosis in uterine serous carcinoma. Lasty, in a recent study published by Jegatheeswaran et al, 36.6% of patients with high-grade endometrial carcinoma had complete surgical staging including para-aortic lymph node sampling and omentectomy but 50.1% had only SLN mapping and pelvic lymphadenectomy, indicating a trend towards omitting para-aortic lymphadenectomy and omental biopsy in high-grade uterine neoplasia. Thus, the low rate of omental and para-aortic sampling in our study is in line with the trend towards less extensive surgical staging and increased use of SLN biopsies in high-risk endometrial cancer.

Table 2  Patients with recurrences

<table>
<thead>
<tr>
<th>Patient</th>
<th>Histology</th>
<th>Polyp</th>
<th>LVSI</th>
<th>Adjuvant treatment</th>
<th>Site of recurrence</th>
<th>Time to recurrence (months)</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Serous</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Vaginal vault</td>
<td>55</td>
<td>ChemoTx, EBRT, BrachyTx</td>
<td>NED 75 months</td>
</tr>
<tr>
<td>2</td>
<td>Serous</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Nodes</td>
<td>15</td>
<td>ChemoTx</td>
<td>NED 41 months</td>
</tr>
<tr>
<td>3</td>
<td>Mixed (serous 10%)</td>
<td>No</td>
<td>Yes</td>
<td>BrachyTx</td>
<td>Lungs</td>
<td>21</td>
<td>ChemoTx</td>
<td>NED 67 months</td>
</tr>
</tbody>
</table>

BrachyTx, brachytherapy; ChemoTx, chemotherapy; EBRT, external beam radiation therapy; LVSI, lymphovascular space invasion; NED, no evidence of disease.

Figure 1  A: Kaplan–Meier for progression-free survival (PFS). B: Kaplan–Meier for overall survival.

Study Strengths and Weaknesses
The strength of our study is that it is a single-center series with a uniform post-operative management and included only patients with disease limited to a polyp or without myometrial invasion. Our study is limited by its small size, its retrospective nature, and relatively short follow-up. However, due to the rarity of this entity, a large prospective study would be hard to conduct. Another limitation of our study is that only 16% of patients had omental sampling and 12% had para-aortic lymph node sampling, which is lower than in previous older studies. However, recent publications have shown that the detection of microscopic disease in normal-appearing omentum is rare in uterine serous carcinoma. Although a recent study showed that the occurrence of omental metastases in patients with serous intraepithelial carcinoma varied from 5.1% to 9.8%, adnexal involvement was found to be an important risk factor associated with omental involvement. Hui et al also showed that when the omentum is involved, it is usually macroscopic disease or there is evidence of metastases elsewhere.

Implications for Practice and Future Research
Although this study was not meant to be a thorough literature review, we identified the largest studies on endometrial carcinoma limited to a polyp or the endometrium. Smaller studies were not all included. Our review highlights the lack of prospective data and uniform management of those patients.

CONCLUSIONS
The findings of our study are concordant with other larger retrospective studies showing that expectant management with surveillance alone appears to be safe for patients with high-grade endometrial carcinoma limited to a polyp or the endometrium without myometrial invasion. Recurrence rate is low and salvage rate following treatment may favorably impact outcomes.

Contributors  MCR and LDN gathered patients’ data. JG did the statistical analyses. LDN wrote the first draft of the article and MP reviewed the article. All authors contributed to study design, data interpretation, critical review of article.
<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th>Inclusion criteria</th>
<th>Adjuvant treatment</th>
<th>Outcome</th>
<th>Conclusion</th>
</tr>
</thead>
</table>
| Nasioudis et al\(^\text{10}\) | Retrospective cohort (n=1709) National Cancer Database (USA) | ► Stage IA  
► Serous carcinoma  
► Limited to a polyp or the endometrium | ► No adjuvant treatment (n=833, 48.7%)  
► CT only (n=353, 20.7%)  
► CT+RT (n=348, 20.4%), 80% brachy only  
► RT only (n=175, 10.2%) | ► Median F/U: 58.55 months  
5-year OS 81.9% in observation group compared with 91.3% in CT+RT and 85% RT only (p=0.001)  
OS better in CT+RT group compared with observation (HR 0.85, CI 95% 0.53–0.88) and CT group (HR 0.64, CI 95% 0.35–0.8)  
► PFS unknown (cause of death N/A in database) | No difference between CT and CT+RT  
Better OS if CT or CT+RT compared with observation |
| Mandato et al\(^\text{12}\) | Retrospective cohort n=75, 66 patients with stage IA | ► Retrospective data from 7 gynecology-oncology centers in Italy  
► Patients with USC confined to a polyp of any stage (88% stage IA) | ► No adjuvant treatment in 50 patients (66.7%)  
► Adjuvant treatment in 25 patients, including 24.2% with FIGO IA  
= RT (4%)  
= CT (88%)  
= Brachy (8%)  
= 12% patients (n=9) upstaged to stage II-IV (all received adjuvant treatment) | ► Median F/U 40 months  
45% had complete surgical staging (including para-aortic LN and omentectomy), 45% had incomplete staging and 13.3% no staging  
Patients with stage IA complete staging and no adjuvant Tx had a risk of relapse of 5.2%  
Patients with stage IA, complete staging, and adjuvant treatment had a risk of recurrence of 12.5% | Complete surgical staging and HTN were associated with lower risk of relapse (especially compared with no staging)  
No impact of adjuvant treatment |
| Boyraz et al\(^\text{13}\) | Retrospective cohort study n=182 patients n=20 for patients with USC confined to the endometrium | Patients with USC confined to the endometrium with or without metastatic disease | ► 20 patients had stage IA confined to the endometrium  
► Observation (70%)  
► Brachy (20%)  
► CT+brachy (5%)  
► CT (5%) | ► Mean F/U 31 months  
6 patients with disease confined to the uterus had adjuvant treatment (30%)  
OS and PFS similar for patients who received adjuvant treatment compared with observation (p=0.25 and p=0.30, respectively)  
► Mean F/U 46.5 months  
5 recurrences:  
= 4 had received adjuvant therapy (3 CT + brachy and 1 brachy)  
= PFS and OS rate at 3 years: 94.9% and 98.8%, respectively | No impact of adjuvant treatment |
| Liang et al\(^\text{9}\) | Retrospective cohort (n=85) | ► Stage IA  
► High-grade EC  
► Limited to a polyp (57.6%) or without myometrial invasion (24.4%)  
► LVSI excluded | ► No adjuvant treatment (23.5%, 9 because of patient refusal)  
► CT±RT (58.1%)  
► Brachy (24.7%) | ► Mean F/U 52 months  
Mean PFS 53.2 and mean OS 68.9 months  
CT did not impact on mean PFS and OS (recurrences of 25.5% vs 26.9%, p=0.8) | No impact of adjuvant treatment |
| Mahdi et al\(^\text{14}\) | Retrospective cohort study (n=115) | ► Stage IA non-invasive USC  
► Surgical staging including pelvic LNP (84%), omentectomy 57%  
► LVSI excluded  
► Brachy (20%)  
► CT (88%)  
► CT only (4%)  
► CT+RT (1.7%)  
► CT+brachy (0.9%)  
► CT+RT+brachy (4.4%) | ► Observation (37.4%)  
► CT (18.3%)  
► CT +brachy (23.5%)  
► CT+RT (7.7%)  
► RT+brachy (4.4%) | ► Mean F/U 68 months  
Mean PFS 53.2 and mean OS 68.9 months  
CT did not impact on mean PFS and OS (recurrences of 25.5% vs 26.9%, p=0.8)  
► Mean F/U 46.5 months  
5 recurrences:  
= 4 had received adjuvant therapy (3 CT + brachy and 1 brachy)  
= PFS and OS rate at 3 years: 94.9% and 98.8%, respectively | No impact of adjuvant treatment |
| van der Putten et al\(^\text{13}\) | Retrospective cohort study (Stage IA without myometrial invasion n=41) | ► USC stage I (at least 10% of serous)  
► Surgical staging with at least a hysterectomy and salpingo-oophorectomy  
– Pelvic LNP in ≥ 66%  
– No omental biopsy in 51.2% | ► Observation (73.1%)  
► Brachy (6%)  
► CT (2.4%)  
► CT+RT (19.5%) | ► Median F/U 54.2 months  
5-year disease-free survival of 80.7%  
Recurrence rate of 12.2%  
= 10% in observation and 18% in adjuvant treatment group (p=0.6)  
= 72.2% of recurrences were distant  
= Few para-aortic and omental recurrences | No impact of adjuvant treatment on outcomes |
| Chang-Halpenny et al\(^\text{13}\) | Retrospective cohort (n=51) | ► Stage IA  
► Serous carcinoma or clear cell  
► Limited to a polyp or the endometrium  
► 5 had myometrial invasion (9.8%) | ► No adjuvant treatment (n=40, 80%)  
► Brachy only (n=1, 2%)  
► Adjuvant treatment if myometrial invasion, positive peritoneal washings, or incomplete staging  
= CT+RT (n=6, 12%)  
= CT (n=3, 6%)  
► Observation (73.1%)  
► Brachy (6%)  
► CT (2.4%)  
► CT+RT (19.5%) | ► Median F/U 45.2 months  
4 recurrences with carcinomatosis or pelvic lymph nodes (7.8%)  
11 deaths: 3 from EC, 2 new gynecologic cancer, 6 from non-malignant conditions  
► PFS and OS at 5 years: 93% and 80.6%, respectively | No impact of adjuvant treatment on outcome |
Original research

Table 3

<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th>Inclusion criteria</th>
<th>Adjuvant treatment</th>
<th>Outcome</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fader et al15</td>
<td>Retrospective cohort (n=54)*</td>
<td>Stage IA</td>
<td>No adjuvant treatment</td>
<td>For the stage IA subgroup:</td>
<td>Impact of adjuvant treatment</td>
</tr>
<tr>
<td></td>
<td>*Entire cohort n=206</td>
<td>Serous carcinoma</td>
<td>(n=21, 38.9%)</td>
<td>Median F/U 27 months</td>
<td>CT (p=0.001) and CT (p=0.0001)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CT (n=28, 51.9%)</td>
<td>6 recurrences (11.1%)</td>
<td>associated with better PFS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Brachy (n=5, 9.3%)</td>
<td>Recurrences: 21.4%</td>
<td>Recurrences: 21.4%</td>
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<td>31.1% in observation group</td>
<td>Recurrences: 31.1%</td>
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<td>38.3% in RT group</td>
<td>RT subgroup</td>
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<td>10.5% in CT group (p=0.001)</td>
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<td></td>
<td></td>
<td>Limited to a polyp or the endometrium</td>
<td>No patients received CT</td>
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<tr>
<td>Dallaire-Nantel et al</td>
<td>Retrospective cohort (n=25)</td>
<td>Stage IA</td>
<td>No adjuvant treatment</td>
<td>Median F/U 44 months</td>
<td>No impact of adjuvant treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Type II endometrial carcinoma</td>
<td>(n=19, 76%)</td>
<td>3 recurrences (12%)</td>
<td>on treatment on outcome</td>
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<td>Limited to a polyp or the endometrium</td>
<td>Brachy (n=6, 24%)</td>
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</tbody>
</table>

brachy, brachytherapy; CI, confidence interval; CT, chemotherapy; CT-RT, chemoradiation; EC, endometrial cancer; FIGO, International Federation of Gynecology and Obstetrics; F/U, follow-up; HR, hazard ratio; HTN, hypertension; LN, lymph node; LNP, pelvic lymph node; LVSI, lymphovascular space invasion; N/A, not available; OS, overall survival; PFS, progression-free survival; RT, radiotherapy; Tx, treatment; USC, uterine serous carcinoma.

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ORCID iD Leonie Dallaire Nantel http://orcid.org/0000-0002-4141-706X

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