

# Tertiary cytoreduction for recurrent endometrial cancer

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## Summary

This paper reviews the surgical approach experiences in endometrial cancer recurrence and presents for the first time data on the surgical management of endometrial cancer patients at the time of their second recurrence. Surgery could represent a pivotal role in selected cases of recurrent endometrial cancer, offering long-term complete remissions and a survival advantage.

*Key words:* Recurrent endometrial cancer; Salvage surgery; Metastasectomy.

## Introduction

Treatment options for recurrent endometrial cancer (EC) patients are radiotherapy, chemotherapy or hormonal modulation, whereas surgery currently only plays a marginal role [1-6]. In the present paper, the authors report convincing survival data in carefully selected EC patients subjected to secondary cytoreduction with distant relapse; furthermore, they present their experience of women subjected to tertiary cytoreductive surgery for recurrent EC.

## Case Report

### Case 1

A 64-year-old woman was referred to the present Institution after having undergone a right salpingo-oophorectomy with pathological diagnosis of endometrioid EC in May 1997. One month later she completed her surgery with an exploratory laparotomy (ELAP), total abdominal hysterectomy (TAH) and left salpingo-oophorectomy. Pathology showed a moderately differentiated endometrioid EC FIGO Stage IIIA. Adjuvant chemotherapy with cisplatin and adriamycin was delivered. The patient recurred six months later with an isolated abdominal recurrence to a para-aortic lymph node. She therefore underwent secondary cytoreduction with ELAP, paracaval lymphadenectomy, partial omentectomy, and partial gastrectomy secondary to disease extension. Macroscopic residual disease was absent and resection margins were negative. Chemotherapy with cisplatin and paclitaxel was delivered. The patient remained disease-free for five years when she recurred again with a single lesion to a para-aortic lymph node in June 2003. She therefore underwent an ELAP and selective left para-aortic lymph node dissection. Pathology showed recurrent EC to one lymph node. Chemotherapy with paclitaxel, adriamycin, and cisplatin was delivered. The patient is currently 81-years-old and free from disease 11 years after her ter-

tiary salvage surgery.

### Case 2

A 71-year-old woman underwent an ELAP, bilateral salpingo-oophorectomy (BSO), omentectomy, and peritoneal biopsies for a FIGO Stage IV endometrioid EC in July 2006. The uterus was not extirpated secondary to involvement of the bladder and rectum. After chemotherapy with paclitaxel, adriamycin, and cisplatin, the patient underwent an ELAP, TAH, and biopsies in March 2007. Macroscopic residual disease was absent. Pathology confirmed a well-differentiated endometrioid EC involving the uterine wall to the serosa and resection margins were negative. No further treatment was recommended. Three years later, PET-CT scan performed for cancer surveillance denoted two areas of metabolic hyperactivity: one in the descending colon and one in the right pelvic lymph nodes. At colonoscopy, a polyp in the descending colon, approximately three-cm distal to the splenic flexure was found and resected. Pathology revealed a colonic adenocarcinoma (pT1G2). She therefore underwent a right hemicolectomy and a right pelvic lymph node sampling in April 2010. Pathology was negative on the large bowel but a recurrent EC was identified in a right pelvic lymph node. Chemotherapy with carboplatin and paclitaxel was delivered. With a PET-CT scan performed more than a year later, further areas of metabolic hyperactivity were noted in the pelvic lymph nodes bilaterally. The patient underwent an ELAP and a systematic pelvic and para-aortic lymph node dissection in November 2011. Pathology revealed a recurrent EC to a left pelvic lymph node. Chemotherapy with carboplatin and epirubicin was delivered. The patient is currently 79-years-old and free from disease eight years after her initial surgery.

### Case 3

A 58-year-old woman underwent an ELAP/TAH/BSO/pelvic lymphadenectomy for an endometrioid EC in December 2004 at a different Institution. Final FIGO Stage was IA. In January 2006 a PET-CT scan revealed metabolic hyperactivity in the pelvis. The

Revised manuscript accepted for publication January 25, 2016

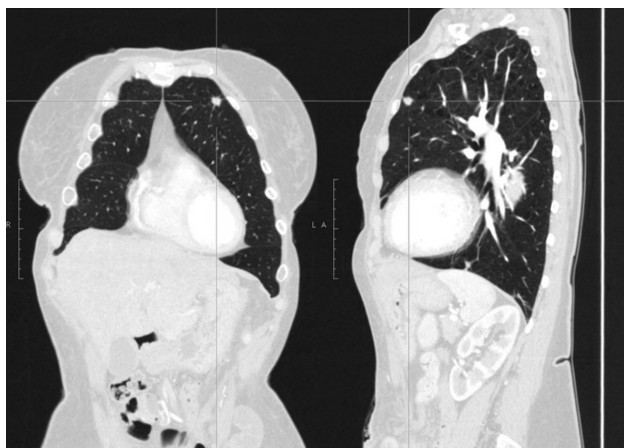


Figure 1. — Isolated pulmonary recurrent endometrial disease documented by CT scan.

patient underwent a diagnostic laparoscopy that confirmed recurrent EC to the pelvis. The patient was then started on chemotherapy with carboplatin, and after three cycles, was referred to the present Institution. A CT scan showed three pelvic masses, the largest of which had a six-cm diameter and was adherent to the rectum. In May 2006 the patient underwent an ELAP, posterior exenteration, colpectomy, and left ureteroneocystostomy with no macroscopic residual disease. Pathology confirmed the diagnosis of recurrent EC to the rectum and the vagina. Margins were negative. No further treatment was recommended. Eight years later, in April 2014, a pulmonary lesion was noted on a chest X-ray. CT scan confirmed the presence of an isolated lesion to the apex of the left lung (Figure 1). PET scan documented that it was metabolically hyperactive. The patient underwent a video-assisted thoracoscopic surgical resection of the apex of the left lung. Pathology revealed recurrent EC with negative resection margins. Nine years after her initial diagnosis, at age 68, the patient is disease-free.

## Discussion

EC benefits from satisfactory survival rates. However, in the majority of the patients affected by disease recurrence, the prognosis is poor. Radiotherapy is able to salvage previously non-irradiated women with vaginal recurrences, but in all other cases, systemic palliative treatments with chemotherapy or hormonal modulation are considered the only option with median overall survival ranging from 9.2 to 15.3 months [7-11].

Historically, the only surgical procedure with curative intent offered to these women was pelvic exenteration [12]. Recently, some pioneristic series have shown unexpectedly high survival rates in women affected by distant recurrences treated surgically, with median survival ranging from 28 to 72 months [1-6].

Finally, these series reported in the first recurrence setting are in line with the present results reported in secondary relapses. Although anecdotal, these three cases support the

hypothesis that women subjected to “beyond” secondary cytoreduction can take benefit from surgery and represent the proof of concept that women can still acquire prolonged disease-free intervals even when affected by recurrent distant disease.

Particularly, from literature data carried out that surgery in recurrent EC is particularly challenging since women affected by this neoplasm, are generally old, obese, and suffer from multiple comorbidities, but the morbidity of surgical procedures in this subset of patients has steadily decreased over time and is now more than acceptable. It is difficult to pin down prognostic factors predicting a successful outcome. However, controlled status of the primary lesion, recurrence outside of an irradiated area, good performance status, long progression-free survival, an optimal cytoreduction with negative margins, and no residual disease seem to be important variables in selecting patients for salvage surgery in this setting. Furthermore, it must be pointed out that response to chemotherapy can have a great variability and that “chemotherapy cures”, although very rare, may occur.

## Conclusion

In the recurrent EC setting, all treatment strategies need to be carefully evaluated. In selected cases, a surgical resection with negative margins may provide symptom relief, long-term complete remission without systemic therapies, and a survival advantage. In this setting, the role of adjuvant systemic chemotherapy is unclear but may help in sterilizing microscopic foci of disease, thus improving the overall outcome.

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