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[Category: Review]

The Role of Surgery in Recurrent Endometrial Cancer

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Abstract

Endometrial cancer is a common gynecologic malignancy in the United States and the recurrence rate depends on stage disease at diagnosis. The spread of the disease at recurrence can occur in several areas and follow different patterns. The role of surgery at the time of recurrence is not clearly defined. The aim of this review is to fully describe the current evidence available on this topic. In particular, we will describe that surgical treatment might be recommended for 1) vaginal or pelvic recurrences; 2) retroperitoneal or localized intra- abdominal recurrence, where a maximal cytoreductive effort is more likely to be successful; or 3) isolated distant recurrences when microscopically tumor-free margins can be achieved. Cases should be evaluated individually, considering factors such as comorbidities, risks of intervention, and impact of treatment on quality of life.

Keywords: endometrial neoplasm; intraoperative radiation therapy; metastases; quality of life; secondary cytoreductive surgery

Introduction

Neoplasms of the uterine corpus are the fourth most common cancer in women. In 2015, an estimated 54,870 new cases of endometrial cancer were diagnosed and 10,170 women died of this disease. From 2007 through 2011, the incidence rate and death rate increased by 2.4% and 1.9% per year, respectively, probably because of higher life expectancy and increasing incidence of obesity in developed countries (1).

Endometrial cancer generally has a favorable prognosis. At diagnosis, most women have early stage, low-grade disease, which is associated with a 90% 5-year survival rate and an estimated recurrence risk of 10% to 15%. However, in women with high-risk histologic findings (grade 3 endometrioid adenocarcinoma, papillary serous, clear cell, and carcinosarcoma histologic subtypes) or locally advanced disease, the biological behavior of the cancer is more aggressive and the prognosis is worse, with recurrence rates as high as 50% (2).

Recurrence typically develops within 3 years of primary treatment (3). After recurrence is diagnosed, the subsequent management strategy depends on the site of recurrence, the duration of the disease-free period, the general medical condition of the patient, and whether prior adjuvant treatment (radiotherapy, chemotherapy, or both) was administered. Patients with local recurrence and no previous radiotherapy often receive radiotherapy, whereas women with disseminated distant metastasis receive systemic treatment (chemotherapy or hormonal therapy). In these settings, the role of surgery is poorly defined and data in the literature are scant. Here, we review the available literature regarding surgical options and their feasibility in recurrent endometrial cancer.

Primary Treatment of Endometrial Cancer

Diagnosis and Staging

Postmenopausal bleeding is the most common symptom of endometrial cancer, and the diagnosis is usually established by endometrial biopsy, or dilatation and curettage, with or without hysteroscopy. For clinical staging, preoperative imaging (eg, computed tomography [CT], magnetic resonance imaging, or positron emission tomography [PET]) is used to determine the presence of extrauterine disease and is generally indicated for patients with symptoms or abnormal clinical findings. Unfortunately, preoperative imaging studies are generally not accurate for detecting microscopic extrauterine metastases (4-6). Surgical staging is the diagnostic criterion standard for the identification of extrauterine dissemination and is a cornerstone of management of endometrial cancer. According to the International Federation of Gynecology and Obstetrics staging system, complete staging consists of hysterectomy and bilateral salpingo-oophorectomy and may also include pelvic and para-aortic lymphadenectomy.

Surgical Approach, Special Situations, and Postsurgical Treatment

Traditionally, staging laparotomy is the surgical approach of choice for endometrial cancer, but recently, laparoscopic or robot-assisted approaches are increasingly used. Randomized controlled trials comparing laparoscopic surgery with laparotomy showed similar surgical effectiveness without compromising the degree of oncologic radicality (7,8). Furthermore, robotic surgery may show outcomes similar to those of laparoscopy (9,10).

Table 1 shows suggested surgical procedures for primary and recurrent endometrial cancer.

After surgical staging, adjuvant therapy (systemic chemotherapy, radiotherapy, or a combination) may be indicated for patients with advanced-stage disease or those with tumors confined to the uterus but with associated risks factors (11).

Patterns of Dissemination and Recurrence

The overall rate of recurrence for endometrial cancer is about 10% to 15%, with more than half of failures occurring within 3 years of primary treatment (3). Recurrence rates are higher in patients with advanced-stage disease and those with aggressive histologic subtypes (grade 3 or nonendometrioid) (3). Most women are symptomatic at the time of recurrence, and the most common symptoms are bleeding (from the vagina, bladder, or rectum), anorexia, weight loss, bone or pelvic pain, cough, shortness of breath, or lower abdominal or extremity swelling (12).

The diagnostic evaluation of suspected recurrent disease includes a pelvic examination with possible biopsies of clinically suspicious areas; a physical examination focused on nodal regions; and radiologic imaging to determine whether metastatic disease is present. CT is often the primary imaging modality used to evaluate potential recurrence; if the scan is equivocal, further evaluation with PET or combined PET-CT may be indicated (11).

Recurrent endometrial cancer disseminates via 4 main routes: contiguous, lymphatic, peritoneal, and hematogenous (Table 2) (14). The pattern of metastasis can be attributed to 1 route alone or a combination. As an example, in an unselected population of 915 patients (without history of

other malignancies) who received treatment for endometrial cancer during a 13-year period, the relapse rates were 5% for vaginal, 9% for hematogenous, 6% for lymphatic, and 6% for peritoneal pathways of dissemination (14) (Figure 1).

From a clinical perspective, recurrence can be organized into 4 patterns:

1. Isolated vaginal recurrence (or central recurrence) is defined as an isolated recurrence involving the vaginal vault or cuff
2. Central pelvic recurrence (or locoregional recurrence) is typically recurrent disease affecting pelvic structures such as the vulva, vagina, lower urinary tract, and rectosigmoid colon
3. Lateral-pelvic recurrence or pelvic sidewall recurrence is a lymphatic recurrence along the major vessels of the pelvic side wall
4. Distant extrapelvic recurrence (eg, in the abdominal retroperitoneum, lung, brain, or other distant sites) is often multifocal

The management strategy for patients with recurrence depends on the site of recurrence, the duration of the disease-free period, the general medical condition of the patient (including Performance Status), and whether prior adjuvant treatment (radiotherapy, chemotherapy, or both) was administered (Figure 2). Women with recurrent disease isolated to the vaginal vault are potentially curable (15). Options for treatment depend on whether radiotherapy was previously administered. If radiotherapy was not administered previously, it is the treatment of choice. If radiotherapy was administered, radical surgery is an option for select candidates. Similarly, in women with locally recurrent disease limited to the central pelvis, treatment options potentially are curative and include surgery or radiotherapy

(including intraoperative radiotherapy [IORT] for lateral recurrences). In women with extrapelvic disease, treatment usually is not curative and the approach should be individualized (11,16).

Despite the above indications, the role of surgery in recurrent endometrial cancer is rarely mentioned in the literature. Current guidelines from the United States (National Comprehensive Cancer Network), Canada (Alberta Provincial Gynecologic Oncology Tumour Team), and Europe (European Society for Medical Oncology) recommend a surgical approach for women with isolated vaginal or pelvic recurrence and a history of radiotherapy, but the recommendation is supported by only low-level evidence (11,16,17). For distant metastases, available data are from case reports or small series, so indications are only weakly supported.

In patients with multiple recurrence sites, usually surgery is not considered as a feasible option. However, in few selected cases, it could be taken into account especially if the performance status of the patients is good and the lesions are resectable with no residual tumor left.

Options for surgical management of endometrial cancer, depending on the pattern of recurrence, are described below. We emphasize that the most favorable surgical candidates have a good performance status and a long interval without endometrial cancer or any other systemic disease; additionally, they must have resectable disease with the potential to achieve microscopically tumor-free margins. A multidisciplinary approach is however mandatory in order to tailor therapies.

Figures from 3 to 6 and Table 3 summarize the surgical options for every site of recurrence.

Isolated Vaginal and Locoregional Recurrence

Women who have undergone surgery for endometrial cancer are at risk of relapse in the vaginal vault; this 8-year risk of relapse is lower in those who received adjuvant external radiotherapy (2% vs 8% for radiotherapy vs no-radiotherapy groups, respectively) or with vaginal brachytherapy (18). Prognosis is usually better in patients with isolated vaginal vault recurrence compared with patients with relapse in other pelvic structures (3-year overall survival rate, 73% vs 8%; $P<.001$) (19).

For patients with a suspected local recurrence (either isolated vaginal or locoregional), radiologic imaging should be performed to exclude other sites of metastasis. The modality considered to be most accurate is integrated PET-CT. If no distant metastases are found, the treatment approach considers whether radiotherapy was previously administered (Figure 3).

Radiotherapy is the standard treatment for women with isolated vaginal recurrence and no history of radiotherapy; the complete response rate is 87% (19). Chemotherapy and surgery can be used in select patients with local extension of the disease or a large-diameter recurrence. For women who have previously received adjuvant radiotherapy, the prognosis is poorer and treatment recommendations vary among institutions. Repeat radiotherapy might be an option in select cases (20), whereas radical surgical resection, sometimes combined with IORT, might be proposed for appropriate surgical candidates (21).

Historically, in surgery-eligible patients with recurrence limited to the vaginal apex within an irradiated field, the surgical approach is pelvic exenteration (22,23). Total exenteration refers to removal of the uterus, fallopian tubes, ovaries (if still present), parametrium, bladder, rectum or

rectal segment, vagina, urethra, and a portion of the levator muscles. In the anterior exenteration, the rectum is spared, whereas in the posterior exenteration, the bladder and urethra are preserved. A perineal phase, with resection of the anus, urethra, and portions of the vulva, may also be required. Other classifications of pelvic exenteration are supralevator and infralevator. Supralevator exenteration includes removal of the bladder, upper vagina, cervix, uterus, and rectosigmoid colon, while preserving the pelvic floor. In infralevator exenteration, removal of the pelvic floor muscles is indicated if the disease involves the lower part of the vagina, vulva, perineum, or anus; reconstruction with myocutaneous flaps, omental flap, or dura mater has been performed to address the large pelvic defect (24).

The choice of procedure depends on the location of the cancer, difficulties that may arise during surgery, type and location of previous radiotherapy, anatomy, and the patient's postoperative goals and expectations. A recent review by Ang et al (25) indicated that no high-level evidence was available to guide women with recurrent cervical, endometrial, vaginal, or vulvar malignancies in decisions about exenterative surgery. No randomized studies have determined whether exenterative surgery is superior to nonsurgical treatment in terms of prolonged survival, treatment-related complications, or quality of life (25).

In a retrospective cohort study of patients who underwent pelvic exenteration after recurrent endometrial neoplasm, Westin et al (26) described a 5-year relapse-free survival rate of 45% and a 5-year overall survival rate of 56%. Other series have described similar 5-year overall survival rates (27-33).

The potential complications after pelvic exenteration are numerous and should be taken into account at time of decision. The major early postoperative complications include blood loss, sepsis, wound dehiscence, and anastomotic breakdown at the level of the bowel, urinary pouch, or ureteral sites.

Late complications include fistula, bowel obstruction, ureteral strictures, renal failure, pyelonephritis, and chronic bowel obstructions.

Other complications include deep venous thrombosis and pulmonary emboli, flap necrosis, and stomal necrosis. (34-35)

Despite improvements in patient selection and surgical techniques, overall survival rates have not changed meaningfully over time, and rates of long-term complications have remained steadily high (26). Therefore, because short- and long-term sequelae of treatments might have a significant and negative impact on a patient's quality of life, and considering that surgical exenteration is a mutilating procedure, great effort should be made in the preoperative setting to accurately inform the patient and provide psychological support.

Lymphatic Spread

Retroperitoneal Disease

Many endometrial cancers recur within the pelvic sidewall or retroperitoneum through lymphatic embolization (Figure 4). Pelvic and paraaortic lymph nodes are most commonly involved in nodal spread. External iliac lymph nodes are the most commonly involved pelvic lymph nodes, followed by the obturator and common iliac nodes. Lymphatic recurrences, which are generally poorly differentiated, do not respond to hormonal therapy and respond poorly to multiagent chemotherapy (18). Recurrence in the pelvic sidewall or lymph node−bearing areas is associated with 3-year sur-

vival rates of less than 10% after radiotherapy, and local secondary recurrence rates may be as high as 100% (18).

A case series of 25 patients with retroperitoneal recurrences, reported an aggressive treatment approach with preoperative radiation, radical surgical resection, and intraoperative radiotherapy (36). The objective was to determine whether this approach maximized tumor control and decreased complications compared with radiotherapy alone. The overall 5-year survival was 47% (median survival, 57 months). Patients with a gross total resection and negative margins had a 5-year survival rate of 71%, which was much better than patients with gross or microscopic residual disease (0% and 40%, respectively). This finding underscores the importance of achieving gross total resection.

The morbidity rate of radical procedures is high (64%) (36). Possible complications include pulmonary embolism, acute lower-extremity ischemia, small-bowel and functional ureteral obstruction, and fistulas. Nevertheless, given that tumor-related mortality rates in the absence of treatment are nearly 100%, radical procedures should be considered; however, their high rates of morbidity must be discussed preoperatively with the patient.

Isolated Distant Nodal Recurrences

First recurrences in an inguinal, axillary, or supraclavicular node as an isolated site are extremely rare. Twenty two patients with such a recurrence were reported in a case series; of these, 7 were treated with excision and aggressive local irradiation and achieved local control of the nodal recurrence. Although the median survival after isolated peripheral lymph node recurrence was only 19 months, 6 patients were alive without

evidence of cancer at a median follow-up of 27 months (37). Even if an associated effective systemic adjuvant treatment is usually needed, in patients with isolated peripheral nodal recurrences, this series showed that aggressive local treatment can provide long-term, disease-free survival.

Peritoneal Recurrences

Peritoneal carcinomatosis is a common type of recurrent endometrial carcinoma (Figure 5), accounting for 28% of relapses. This pattern of recurrence is generally associated with a poor prognosis (14,38). Recurrences may be large peritoneal masses, peritoneal nodules, and serosal implants that may cause extrinsic compression of the bowel.

The meta-analysis by Barlin et al (39) suggests that among patients with recurrent or advanced endometrial cancer, surgical cytoreduction to no gross residual disease may confer a survival advantage. Papadia et al (40) reported complete resection to no visible disease in 42 of 64 cases of EC (66%) that underwent cytoreductive surgery for recurrence, and according to the studies considered in the review by Barlin et al (40), they reported similar 5-year rates of RFS and OS (34% and 51%, respectively).

Any residual disease (microscopic or gross) after cytoreductive surgery is considered a failed surgical treatment. Some patients with microscopic residual disease have undergone cytoreductive surgery and received hyperthermic intraperitoneal chemotherapy; however, available data are based on only a few patients, and no consistent conclusion about the benefits of this procedure can be drawn (41).

In conclusion, cytoreductive surgery in peritoneal recurrences is indicated if patient has a good preoperative performance status without comorbidities that might contraindicate the procedure itself, and if complete resection of

macroscopic disease is achievable. When complete removal of the disease is not achievable but a maximum extent of surgery will improve patients quality of life (for example, in cases of bowel obstruction), surgical approach is indicated as a palliative treatment.

Hematogenous Dissemination

Hematogenous recurrence can affect the brain, lungs, liver, and bone (Figure 6).

Lung

The incidence of pulmonary metastasis for patients with endometrial cancer ranges from 2.3% to 7%. Stage IV disease and myometrial invasion exceeding 50% are the strongest predictors of lung failure. Nodules are frequently multiple and bilateral, but a solitary nodule may also occur.

With lung metastases, the prognosis is generally poor. However, hematogenous dissemination to the lungs tends to occur in elderly patients with low-grade tumors; this finding might indicate a spectrum of tumor behavior, with lung metastasis indicating less-aggressive behavior compared with tumors having hematogenous dissemination to other sites (42). Criteria for determining eligibility for surgical resection of pulmonary metastases are shown in the Box.

From the literature, predictors of survival in patients with isolated lung metastases are length of the disease-free interval and number of cancerous pulmonary nodes. In a series of 28 cases, the following characteristics predicted favorable outcome: grade 1 or 2 tumors, greatest diameter of pulmonary nodule ≤2 cm, nonchemotherapy treatment, and

estrogen receptor−positive status. Although chemotherapy was associated with reduced survival, outcomes were similar among patients treated with surgical resection vs those receiving progestational therapy. Considering the most favorable risk:benefit ratio of administration of progestational therapy vs thoracotomy, hormonal therapy is a reasonable consideration, at least as a first-line treatment for patients with low-grade tumors (43).

Even if data in the Literature are available on the role of stereotactic radio surgery in primary lung cancer, only very limited information is available on its role in metastatic or recurrent gynecologic cancer. for this reason, no conclusions can be drawn about efficacy and long term effects. (44)

Bone

Bone metastases in endometrial cancer are less common, with an overall incidence rate less than 1%. The spine and hip are the most common sites of osseous dissemination, and the 5-year survival rate after diagnosis of bone dissemination is extremely poor (1%) in the setting of recurrent disease. However, the prognosis is better when bone metastases are discovered at presentation (45).

No consensus exists on the best elective treatment of bone metastases, and multimodal therapies are usually administered. Surgery can be considered for patients with impending or existing pathologic fractures, spinal cord compression, and pain, especially in the setting of resistance to radiotherapy. Surgical options include 1) wide resection (consisting of en bloc removal of the bone lesion with an envelope of normal tissue, followed by reconstruction); 2) intralesional curettage followed by internal fixation; and 3) palliative decompression of the spinal cord (46).

Although surgical excision of the metastasis is an option, little in the literature describes the impact of this treatment on survival. Thus, no definite conclusions can be drawn, and multimodal therapies are usually required.

Brain

Brain metastases in patients with endometrial cancer are rare (estimated prevalence, 0.86%). Prognosis is poor, and the median overall survival after diagnosis is 6.5 months (unpublished data). Because of the low prevalence of brain metastasis, radiologic examination of the brain is not universally recommended for patients with endometrial cancer. Diagnosis is usually established by imaging tests after the onset of symptoms (eg, limb paresis, refractory headache).

During the past decade, we have observed a controversial evolution in the treatment of brain metastasis. Previously, surgical resection followed by whole-brain radiotherapy (WBRT) was considered the best treatment for a solitary metastasis (47). Moreover, WBRT was used in all patients with brain metastases, independent of the number of metastases. However, because of its detrimental effects on cognition and quality of life, during the past few years, the role of WBRT has been questioned, and some have suggested stereotactic radiosurgery to treat patients with limited brain metastasis (48). Furthermore, a recent multicenter prospective study concluded that stereotactic radiosurgery alone should be considered in patients with up to 5 to 10 brain metastases (49). In contrast, other authors still recommend WBRT with surgical resection in patients with good performance status and limited extracranial disease (50,51). Thus, given the recent considerations, the role of the surgery now is limited to 2 main

indications: 1) to confirm the diagnosis when it is in doubt and 2) to alleviate the mass effect in patients with large tumors. The treatment of brain metastasis should be individualized on the basis of the burden of disease at diagnosis and by considering how to minimize cognitive dysfunction and negative effects on quality of life, without affecting survival outcome.

Liver and Intra-abdominal Organs

The most common intra-abdominal organ affected by hematogenous endometrial metastasis is the liver (7%), followed by the adrenal glands and the spleen (1%) (38). Indications for hepatic resection of gynecologic tumors generally are the same as those for the resection of colorectal metastases: 1) the patient must be medically fit to undergo major abdominal surgery; 2) unresectable extrahepatic tumors must not be visible with preoperative imaging; and 3) grossly negative resection margins must be achievable while still leaving an adequate volume of functional liver.

Because most hepatic recurrences are generally associated with other distant disease (42), few reports have described hepatic metastases resection and splenectomy in the setting of recurrent endometrial cancer. Thus, no definitive conclusions can be drawn about the efficacy of the procedure in terms of survival. Also, multimodal therapy should be delivered after the procedure because occult microscopic systemic dissemination of the disease might be present (52).

Expert Commentary

Treatment options for patients with recurrent endometrial cancer include radiotherapy, chemotherapy, hormonal therapy, and surgery, depending on the type and localization of the recurrence, patient functional status, presence of other associated disseminated disease, duration of the

disease-free survival period, and the intent of the treatment itself (ie, curative or palliative). Data from retrospective series suggest that surgery can be considered for select patients with recurrent endometrial cancer. The main factor to consider when evaluating a patient's eligibility for surgery is the feasibility of completely resecting the disease. Even if subsequent systemic treatments are administered after surgery, the prognostic factor with the greatest effect on survival rates is complete resection of the lesions (including resection of associated distant residual disease). Complete cytoreduction can be achieved in many patients with a single isolated metastasis (even at distant sites), but it may be more difficult to achieve in patients with diffuse intraperitoneal or retroperitoneal disease. Furthermore, because patients with recurrent endometrial cancer usually are affected by several comorbidities, an accurate preoperative evaluation must be undertaken to appropriately weigh the possible risks to the patient if radical surgery is planned. Quality of life should also be considered for the more radical procedures.

Five-Year View

Our recommendation for surgery in recurrent endometrial cancer is mostly limited to patients with locoregional relapse, especially those who previously received radiotherapy. The surgical excision of disease located in other areas is often more dependent on physician preference or surgical skill than on evidence-based indications. In fact, some patterns of recurrence are extremely rare, and evidence-based recommendations do not exist. Ideally, the complete eradication of the disease at relapse should be achieved with minimal impact on the patient's quality of life. A multimodal approach that integrates highly skilled surgery, radiotherapy, and medical therapy can be

considered; such an approach also should be investigated in future research. Tailoring adjuvant therapies to tumor and patient characteristics, possibly with molecular-based therapy, must be the goal of future research (53).

Key Issues

- Endometrial cancer has 4 pathways of dissemination (contiguous, lymphatic, hematogenous, and peritoneal)
- The pattern of recurrence, patient functional status, and prior adjuvant treatment status are instrumental for defining the optimal management strategy and determining the need for surgery
- If surgery is performed for recurrent endometrial cancer, the aim should be macroscopic complete resection
- After local recurrence, surgical resection (pelvic exenteration) is indicated in operative candidates; usual candidates for exenteration are patients who previously received radiotherapy and present with isolated central local recurrence
- In patients with retroperitoneal or intraperitoneal recurrence, cytoreductive surgery with maximum effort to no residual disease improves overall survival
- Intraoperative radiotherapy may be useful in patients with retroperitoneal recurrence; in fact, recurrences affecting the large pelvic or para-aortic vessels are more likely to be excised, leaving microscopic or macroscopic residual disease
- In distant recurrences (eg, bone, brain, lung, liver), surgical resection is feasible in select patients with limited disease; however, no evidence-based data suggesting improvement of survival are available

- Morbidity rates and quality of life must always be considered before radical surgery is performed
- Randomized trials in surgery for recurrent endometrial cancer are certainly needed but are difficult to perform; thus, a homogeneous case series of patients (homogenous in terms of patients characteristics, disease characteristics, and standardized uniform treatment) may help define the best treatment

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Table 1. Surgery in EC

Type of Surgery	Procedure
Primary surgery	
Type 1 endometrioid cancer	Total hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy (depending on preoperative and intraoperative findings), biopsy of any suspect lesions Peritoneal cytology (optional)
Type 2 EC	Peritoneal biopsies, total hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy, omentectomy, biopsy of any suspect lesions
At recurrence	Total pelvic exenteration (or radical pelvic surgery) Surgical cytoreduction to no gross residual disease Surgical excision of isolated distant metastases

Abbreviation: EC, endometrial cancer.

Table 2. Patterns of Recurrence

Recurrence Type	Affected Area
Contiguous	
Isolated	Vaginal vault, vaginal cuff
Local extension beyond the uterus (locoregional)	Vagina, vulva, lower urinary tract, rectosigmoid colon
Lymphatic	
General	Retroperitoneum
Spread through the lymphatic system	Pelvic and para-aortic nodes, inguinal nodes, axillary nodes, supraclavicular nodes, mediastinal nodes
Peritoneal (or spread along the peritoneal cavity)	Intraperitoneal implants, peritoneal carcinomatosis
Hematogenous (or spread through the vascular system)	Most commonly lung, brain, bones, liver

Box. Criteria for Determining Eligibility for Surgical Resection of Pulmonary Metastases

1) The primary tumor site should be free of disease
2) Metastases should be confined to the lungs
3) Total removal of disease must be feasible (the absolute number of metastases per se is not discriminatory)
4) Chemotherapy or hormonal therapy will not be curative, and other more effective therapies are unavailable
5) The patient can tolerate surgical therapy, and pulmonary function is compatible with the proposed resection
6) Total removal of all disease must be possible

(Adapted from Dresler and Goldberg. Surgical management of lung metastases: selection factors and results. Oncology [Williston Park]. 1996 May;10[5]:649-55. Used with permission.)

Legends

Figure 1. Patterns of recurrences in endometrial cancer. Of all recurrences, 48% had a hematogenous component (21% were isolated hematogenous recurrences), 32% had lymphatic component (16% were isolated lymphatic recurrences), 33% had peritoneal component (18% were isolated peritoneal recurrences), and 18% had isolated vaginal recurrences. Approximately 27% of recurrences had multiple components of recurrence. Adapted from Mariani et al (17). Used with permission.

Figure 2. Treatment options for locoregional recurrences. IORT indicates intraoperative radiotherapy; PET-CT, positron emission tomography−computed tomography; RT, radiotherapy.

Figure 3. Summary of surgical options, inclusion criteria, recommendation grade, and other treatments for contiguous recurrences. CHT indicates chemotherapy; EBRT, external beam radiotherapy; GoR, grade of recommendation; HIPEC, hyperthermic intraperitoneal chemotherapy; IORT, intraoperative radiotherapy; PET-CT, positron emission tomography−computed tomography; RT, radiotherapy.

Figure 4. Summary of surgical options, inclusion criteria, recommendation grade, and other treatments for lymphatic recurrences. Abbreviations are defined in the Figure 3 legend.

Figure 5. Summary of surgical options, inclusion criteria, recommendation grade, and other treatments for peritoneal recurrences. Abbreviations are defined in the Figure 3 legend.

Figure 6. Summary of surgical options, inclusion criteria, recommendation grade, and other treatments for hematogenous recurrences. Abbreviations are defined in the Figure 3 legend.