Surgical Staging of Endometrial Cancer

I. Endometrial Cancer – Surgical Staging Overview

- Uterine cancer types: carcinomas – type I and type II, sarcomas, carcinosarcomas
- Hysterectomy with BSO
- Surgical Staging

Malignant tumors of the uterus are broadly divided into three main types: **carcinomas, sarcomas, and carcinosarcomas**. Overall, women have a 2% lifetime risk of developing one of these tumors. Carcinomas account for about 95% of all diagnoses. The term '**endometrial cancer'** usually refers to all the different types of carcinomas.

Endometrioid adenocarcinoma is the most common histologic type of endometrial cancer, accounting for more than 75-80% of cases. This tumor characteristically arises from atypical endometrial hyperplasia and contains glands that resemble the normal lining of the uterine cavity. These **'type I'** cancers are usually grade 1 or 2 (out of 3), have an indolent pattern of myometrial invasion, and a propensity for lymphatic metastases. **Uterine papillary serous carcinoma** (UPSC) and **clear cell carcinoma** comprise 10-15% of all endometrial cancers. These much more aggressive **'type II'** tumors are invariably grade 3 and often behave clinically like epithelial ovarian cancer. As a result, they have a tendency to spread quickly and implant anywhere within the abdomen. Intraoperatively, it is often difficult to confirm with certainty whether a type II endometrial cancer arose from the uterus or the ovary.

Uterine sarcomas usually arise from either the smooth muscle (leiomyosarcoma) or stromal tissue within the endometrium (endometrial stromal tumors). Carcinosarcomas are mixed tumors also known as malignant mixed mullerian tumors (MMMT). In general, these are very aggressive tumors, like UPSC and clear cell carcinomas.

Patients with endometrial cancer have the highest chance of cure by undergoing hysterectomy with bilateral salpingo-oophorectomy (BSO). Only a few circumstances contraindicate primary surgery and include a desire to preserve fertility, massive obesity, high operative risk, and clinically unresectable disease. In general, an extrafascial ('simple') hysterectomy is sufficient, but radical hysterectomy may be preferable for patients with clinically obvious cervical extension of endometrial cancer. Vaginal hysterectomy with or without BSO is another option for those women who cannot undergo systematic surgical staging due to co-morbidities.

The principles of endometrial cancer **surgical staging** are mainly utilized for type I endometrioid adenocarcinomas. Surgical staging involves additional techniques that ultimately may or may not detect metastatic disease. This is very useful information for guiding further therapy. For example, patients who undergo appropriate surgical staging and have no detectable metastatic disease usually DO NOT require any further chemotherapy or radiation. Patients with detectable metastases DO need further non-surgical treatment. There is a dilemma among those patients who have a hysterectomy and BSO for endometrial cancer, but do not undergo surgical staging because there is no other way of reliably discerning

whether metastases are present. These are the general principles that emphasize the importance of surgical staging. Although the same techniques can also be employed for patients with type II UPSC or clear cell carcinomas, often the steps are somewhat modified.

Surgical staging is best performed by a gynecologic oncologist who is trained in all of the procedures, their indications, and the nuances of the particular uterine tumors. **In general, the steps include peritoneal washings, abdominal exploration, hysterectomy with BSO, and pelvic and paraaortic lymphadenectomy for type I tumors. Extended surgical staging, to additionally include partial omentectomy and peritoneal biopsies is indicated for patients with type II endometrial cancer.**

Postoperatively, patients with endometrial cancer are assigned a disease stage using the FIGO system (Table 1). Almost three quarters of type I patients are stage I at diagnosis. Since there is no specific staging system for uterine sarcomas or carcinosarcomas, most clinicians use the same endometrial cancer surgical staging system for these tumors as well.

II. About the steps

- Systematic approach
- Laparotomy or laparoscopic surgery
- Sequence: washings, exploration, hysterectomy with BSO, pelvic lymphadenectomy, paraaortic lymphadenectomy
- Extended staging: omentectomy, peritoneal biopsies

Successful surgical staging of endometrial cancer requires a **systematic, consistent approach**. The sequence of steps is very important. Additionally, the surgeon must be flexible enough to modify the procedure based on the intraoperative findings. Type I endometrioid tumors and its variants most commonly spread, in order of frequency, by: 1) direct extension, 2) lymphatic metastasis, 3) hematogenous dissemination, and 4) intraperitoneal exfoliation. Type II UPSC and clear cell carcinomas have a particular propensity for extrauterine disease. The various patterns of spread are interrelated, and often develop simultaneously.

The operation begins with a decision about whether the patient is a candidate for **laparotomy or minimally invasive laparoscopic surgery**. If a laparotomy is chosen, then the type of incision should be selected next. Surgical staging can be adequately performed by either method, but patients with obvious metastases generally require laparotomy.

Peritoneal washings are collected immediately after entering the abdominal cavity. The reasoning is that the discovery of free-floating malignant cells is most valuable before there is any disruption of the abdominal or pelvic organs. For example, there might be a metastatic ovarian cyst that is ruptured during exploration or surgical removal. This could complicate the clinical interpretation if washings are obtained after this inadvertent event.

Exploration of the abdomen and pelvis is performed next. This is a systematic palpation of all peritoneal surfaces and the uterus with attached adnexa. The rationale is to give the surgeon a sense of the extent of any metastases and guide the operation. For example, palpation of an omental tumor may represent stage IVB disease and make it unnecessary to perform a pelvic/paraaortic node dissection.

Hysterectomy with BSO is usually the next step in the operation. Typically this is performed in a way that facilitates the subsequent node dissection. The hysterectomy/BSO removes the primary tumor source and may provide additional information about how next to proceed. The uterus is opened away from the operating table, and the depth of myometrial penetration may be determined by intraoperative gross examination or microscopic frozen section. In general, the deeper the invasion, the higher the risk for metastatic spread and the more important it is to perform a complete surgical staging procedure. Additionally, if features of type II UPSC or clear cell carcinoma are suspected, it might indicate the need for extended staging with partial omentectomy and peritoneal biopsies. Historically, the combination of preoperative biopsy grade and intraoperative assessement of the depth of myometrial invasion were the two factors that a surgeon used to determine whether to proceed with lymph node dissection. However, recent studies have changed the paradigm. This approach is inconsistent and frequently inadequate. It is difficult to predict with certainty the final histologic grade based

on the preoperative biopsy or intraoperative frozen section. In addition, the depth of myometrial invasion determined in the operative room is often inaccurate. As a result, **complete surgical staging with pelvic and paraaortic lymphadenectomy is recommended for all patients with endometrial cancer**. At a minimum, any suspicious pelvic or paraaortic lymph nodes should be removed.

Pelvic lymphadenectomy is performed first, followed by **paraaortic lymphadenectomy**. The lymphatic network draining the uterus is complex, and patients can have metastases to any single nodal group as well as combinations of groups. This haphazard pattern is in contrast to cervical cancer, in which lymphatic spread usually follows a stepwise progression from pelvic to paraaortic to scalene nodal groups. If firm, matted nodes are identified, they should be removed if possible, sent for frozen section, and completion of the remaining lymphadenectomy may not be necessary if the results demonstrate metastases.

Those patients with type II UPSC or clear cell features on preoperative biopsy should have **extended surgical staging with a partial omentectomy and peritoneal biopsies**. As in ovarian cancer, the surgeon should also be prepared to resect any metastases.

An alternative method of endometrial cancer surgical staging combines a laparoscopic approach to both hysterectomy and lymphadenectomy. In general, this approach is best suited to a select group of women with clinical stage I disease. However, laparoscopic pelvic and paraaortic lymph node dissection may also be an attractive option in women incompletely staged at their primary surgery. The potential benefits of minimally invasive surgery are numerous. Patients have fewer blood transfusions, shorter hospital stays, lower perioperative morbidity, and better quality of life. Disadvantageously, surgical time is typically prolonged, exposure may be limited, limitations or bleeding may require conversion to laparotomy, and staging may be incomplete. However, in selected patients, approximately 70 percent of planned cases can be completed successfully. Overall survival and recurrence rates in early reports are similar to a traditional abdominal approach.

The staging laparotomy described for endometrial cancer can be revised in several ways to incorporate the unique spread patterns of uterine sarcoma. For instance, peritoneal washings may be easily obtained upon opening the abdomen, but have limited value regardless of the result. Exploration is particularly important to assess the abdomen for unresectable or widely metastatic disease that might indicate a need to abort the procedure. Unlike endometrial carcinomas, there is no benefit to aggressive cytoreductive surgery. Uterine leiomyosarcoma and endometrial stroma sarcoma patients should undergo a hysterectomy and usually BSO, but fewer than 5 percent will have nodal metastases. As a result, lymph node dissection should be reserved for patients with clinically suspicious nodes. For uterine MMMT, hysterectomy and BSO is mandatory. Lymph node metastases develop in 15 to 20 percent of patients with clinical stage I disease, and thus, pelvic and paraaortic lymphadenectomy is more valuable. Typically, disease spread is due to the carcinomatous serous or clear cell element. Accordingly, extended surgical staging with partial omentectomy and random peritoneal biopsies is also advisable.

III. Peritoneal washings

- Peritoneal washings

Upon entering the peritoneal cavity, **washings** are obtained by pouring 50 to 100 mL of saline into the abdomen, manually circulating the fluid, and collecting it for cytologic assessment. Retrieval of ascitic fluid is a perfectly acceptable alternative, but ascites is infrequently encountered.

IV. Pelvic nodes

- Pelvic nodes
- Anatomical boundaries

There are no strict, uniform criteria for how many lymph nodes need to be removed to constitute an adequate lymphadenectomy. The Gynecologic Oncology Group (GOG) Surgical Procedures Manual is one benchmark. According to the GOG, the surgeon must remove at least 4 nodes from each side (8 total) for the procedure to be considered a **pelvic lymphadenectomy**. During the operation, it is impossible to tell how many nodes are being removed, because they come in various sizes and are within a fat pad of surrounding adipose tissue. Further, the nodes are counted by a pathologist and there are potential inconsistencies in how the tissues are processed to evaluate the lymphatic tissue. Additionally, there are patient-to-patient variability in the number of nodes.

Therefore, the **anatomical boundaries** are the only real gauge for the surgeon to assess the completeness of the nodal removal. Higher counts (i.e., more than 11-12) correlate with improved survival, most likely due to increased accuracy in finding nodal metastases. In addition, evidence suggests the possibility of a therapeutic benefit for a more comprehensive lymphadenectomy. Removal of grossly involved lymph nodes leads to a survival advantage. Moreover, microscopic nodal disease may be unknowingly resected, thus preventing future relapse.

V. Paraaortic Nodes

- Paraaortic nodes
- Complications

Similar to pelvic lymphadenectomy, there are no strict, uniform criteria for how many lymph nodes need to be removed to constitute an adequate procedure. According to the GOG, the surgeon must remove identifiable 'lymphatic tissue' from each side (2 total) for the procedure to be considered a **paraaortic lymphadenectomy**. Typically, the nodal counts are lower than the pelvic procedure. The paraaortic area is more difficult to reach and may not be completely accessible with all incisions (i.e., Pfannenstiel), bleeding is more common, postoperative complications are more likely (i.e., ileus), and patient factors (i.e., massive obesity) may make it more problematic to perform an adequate lymphadenectomy. For any combination of these or other reasons, paraaortic lymphadenectomy is performed as the last step in routine endometrial cancer surgical staging.

VI. Partial omentectomy

- Partial omentectomy

Type II UPSC or clear cell carcinomas warrant **extended staging** because of their tendency to spread throughout the peritoneal cavity. As in epithelial ovarian cancer, the **omentum** is the most logical and most accessible organ to remove first. If the operation has been performed through laparotomy, then usually the retractor is removed, all abdominal packs are taken out, and the omentum can be pulled through the incision. A portion of the infracolic omentum can be quickly resected and is an excellent test for the presence of microscopic disease spread. Any metastatic tumor, even if microscopic, results in the patient being assigned FIGO stage IVB. This is a reason to initiate systemic chemotherapy postoperatively that otherwise would be missed if partial omentectomy were left out of the staging procedure.

VII. Peritoneal Biopsies

- Peritoneal biopsies

To adequately assess the peritoneum for microscopic disease in type II UPSC/clear cell carcinomas, **bilateral biopsies** are performed of **the pelvis, pericolic gutter and diaphragm**. These six biopsies from both sides and cephalad to caudad within the abdomen should accurately detect any microscopically implanted tumor cells that may not be identified within the omentum.

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