Marguerite Bride. *Barn Light.* Watercolor, 12″ × 18″.

The effects of surgical staging in endometrial cancer on overall survival, utilization of radiation therapy, and impact on quality of life are discussed.

The Role of Comprehensive Surgical Staging in Patients With Endometrial Cancer

Peter J. Frederick, MD, and J. Michael Straughn, Jr, MD

Background: *The cornerstone of the management of patients with endometrial cancer is hysterectomy. Since 1988, the role of lymphadenectomy for patients with endometrial cancer has been debated. Patients who undergo pelvic and para-aortic lymphadenectomy are more likely to be accurately staged and are less likely to receive adjuvant radiation therapy.*

Methods: *The authors perform a narrative review of the recent literature. Overall survival, utilization of radiation therapy, impact on quality of life, and alternative approaches to surgical staging are discussed.*

Results: *Although a survival benefit from comprehensive surgical staging has not been clearly demonstrated in patients diagnosed with endometrial cancer, surgical staging allows one to determine the need for adjuvant therapy. Preoperative and intraoperative assessment of lymph node metastasis and tumor grade lacks accuracy. Unstaged patients are more likely to receive postoperative radiation therapy.*

Conclusions: *Comprehensive surgical staging with lymphadenectomy allows patients to be classified accurately into risk categories. Risk status can be definitively determined only with final pathology. Surgically staged patients are more likely to receive appropriate adjuvant therapy or observation when warranted.*

Introduction

Endometrial cancer is the most common gynecologic malignancy in the United States, with an estimated 40,100 new cases and 7,470 deaths occurring in 2008.[1] Accounting for 6% of all cancers in females, endometrial cancer is predicted to be a continuing problem in the future due to an aging population and an alarming obesity epidemic. Patients commonly present with postmenopausal bleeding, and those with stage I endometrial cancer generally have an excellent prognosis. The 5-year relative survival rate for stage I disease is 97.4%.[2]

Surgical evaluation and staging have been the cornerstone of management since 1988, when the International Federation of Gynecology and Obstetrics (FIGO) system was changed from clinical to surgical staging. Staging includes peritoneal washings for cytology, careful exploration of the abdomen and pelvis with biopsy of any suspicious lesions, total hysterectomy, bilateral salpingo-oophorectomy, and pelvic and para-aortic lymphadenectomy. The method and extent of lymph node

From the Department of Obstetrics and Gynecology, Division of Gynecologic Oncology, at the University of Alabama at Birmingham, Birmingham, Alabama.

Submitted May 1, 2008; accepted August 26, 2008.

Address correspondence to Peter J. Frederick, MD, University of Alabama at Birmingham, Department of Obstetrics and Gynecology, Division of Gynecologic Oncology, 619 19th Street South, OHB 538, Birmingham, AL 35249-7333. E-mail: pfred@uab.edu

dissection have not been uniformly defined and remain controversial. In seeking the optimal care for women with endometrial cancer, the aim is to avoid both overtreatment (ie, sparing a patient unnecessary surgery or radiotherapy) and undertreatment (ie, not treating a patient with occult involvement of her lymph nodes). This review discusses the controversies of lymphadenectomy in patients diagnosed with endometrial cancer.

The Controversy

Multiple issues influence a surgeon's decision to perform comprehensive surgical staging in patients with endometrial cancer. Does surgical staging provide an overall survival benefit? Should all patients diagnosed with endometrial cancer undergo comprehensive staging? Is there an impact on quality of life? Does sparing the patient the morbidity of unnecessary adjuvant treatment outweigh the morbidity of the staging procedure itself? Is comprehensive surgical staging cost-effective? Does the increased use of laparoscopy and minimally invasive surgery lessen the morbidity or influence the cost-effectiveness of surgical staging? Are less invasive diagnostic procedures such as ultrasound, magnetic resonance imaging (MRI), and positron-emission tomography/computed tomography (PET/CT) accurate enough to replace surgical staging in carefully selected patients? Unfortunately, the answers to all of these questions remain unclear. In this review these important issues are examined.

Predictors of Lymph Node Metastases

Several histopathological and clinical risk factors have been identified that predict the likelihood of lymph node metastasis. In the Gynecologic Oncology Group study GOG-33, patients with clinical stage I endometrial cancer were surgically staged and were stratified into three risk categories. High-risk patients were defined as having either deep myometrial invasion or intraperitoneal disease. Patients with deep myometrial invasion had an 18% risk of pelvic node metastasis and a 15% risk of para-aortic lymph node metastasis. Intermediate-risk patients, defined as grade 2 or 3 histology and/or inner-mid myometrial invasion, had a 2% to 6% risk of nodal metastasis. Low-risk patients, with grade 1 histology and endometrial involvement only, had no lymph node metastasis in this study.[3] Other studies have demonstrated an incidence of pelvic lymph node metastasis as high as 4% in low-risk patients with no myometrial invasion.[4] Subsequently, GOG-99 refined the definition of intermediate-risk disease to account for additional prognostic factors such as patient age and the presence of lymphovascular invasion.[5]

Clinical staging has been deemed insufficient because it fails to identify all patients with advanced disease. This is important both for prognostic and therapeutic reasons. Prognostically, patients with lymph node metastasis have worse outcomes; stage III patients have 5-year relative survival rates of 59.6% compared with 97.4% for patients with stage I disease.[2] Therapeutically, studies have demonstrated that surgical excision of grossly involved lymph nodes is associated with improved disease-specific survival.[6,7] Most agree that patients with aggressive histological features, such as clear cell and papillary serous carcinomas, should be comprehensively staged with lymphadenectomy and omentectomy. These patients are more likely to have distant metastases and recur even when the tumor is grossly confined to the endometrium.[8,9]

Preoperative Evaluation

A patient's risk status can be definitively determined only postoperatively. Since certain pathologic factors are unavailable or inaccurate preoperatively or intraoperatively, it may be difficult to determine which patients to select for lymphadenectomy. Preoperative histology obtained from endometrial biopsy or dilation and curettage often differs from final pathology. In a study of 291 endometrial cancer patients by Goudge et al,[10] 18% of tumors were upgraded on final pathology. Similarly, Ben-Shachar et al[11] reported that final pathology was upgraded in 19% of 181 patients with a preoperative grade 1 tumor.

As imaging modalities become more sophisticated, there is hope that a non-invasive scan can provide information concerning the status of the lymph nodes. However, results to date have been disappointing. CT scans have poor sensitivity and specificity in detecting the depth of myometrial invasion, cervical and parametrial involvement, and lymph node metastases.[12] MRI is more accurate than CT scans, with an overall staging accuracy of 85%.[13] However, MRI was only 54% sensitive in determining deep myometrial invasion and had limited specificity for detecting pelvic and para-aortic node metastases.[13] In a more recent study comparing MRI with PET/CT, Park et al[14] demonstrated that PET/CT had a sensitivity of 69.2%, specificity of 90.3%, positive predictive value of 42.9%, and negative predictive value of 96.6%. Although these results were statistically comparable to MRI, it does not appear that PET/CT can replace surgical staging.

Intraoperative Evaluation: Lymph Node Palpation and Frozen Section

Neither lymph node palpation nor frozen section is an accurate method for assessing lymph node metastases. Palpation of lymph nodes is unreliable primarily because many positive lymph nodes are grossly normal. In a study by Girardi et al,[15] 37% of node metastases were less than 2 mm and only 7% were larger than 2 cm. Arango et al[16] published a 36% false-negative rate for intraoperative palpation in 126 women with gynecologic cancers. Similarly, Eltabbakh[17] noted a 26%

false-negative rate for palpation in 178 consecutive gynecologic patients undergoing lymphadenectomy.

In a prospective study comparing frozen section and final pathology for histologic grade and depth of myometrial invasion, Case et al[18] found that frozen section correlates poorly with final pathologic diagnosis. Agreement between frozen and permanent section was seen in only 67% of specimens for depth of invasion and in 58% of specimens for tumor grade. The authors concluded that clinically relevant upstaging occurred in 18% of patients who underwent lymphadenectomy. Therefore, it has been argued that comprehensive surgical staging should be performed on all patients to provide the physician with accurate information to recommend the most appropriate adjuvant therapy.[19]

Proponents of a more selective approach to surgical staging have countered that the incidence of nodal involvement and extrauterine disease is too low to warrant surgical staging on all patients.[20] It has been estimated that 5% of low-risk patients will have extrauterine disease and/or nodal involvement. Additionally, it has been argued that the discrepancy between frozen section and final pathology rarely results in a clinically significant change. For example, changing the grade of a non-invasive endometrial cancer would not alter the overall management or outcome of the patient.

Impact on Overall Survival

When determining whether or not to perform routine lymphadenectomy, a key issue that must be considered is if lymphadenectomy improves outcomes in a patient population that has excellent disease-free survival. Multiple studies evaluating this issue have arrived at contradictory results, largely due to differing study designs, patient populations, and inclusion criteria.

Belinson et al[21] reported on 216 patients with clinical stage I adenocarcinoma of the endometrium who did not receive routine pelvic lymphadenectomy. Paraaortic nodes were dissected only when they were determined to be clinically abnormal, when there was greater than one-third myometrial invasion on frozen section or when there was evidence of cervical or intraperitoneal disease. Over a 5-year follow-up period, 21 patients had a recurrence. Two patients had a pelvic recurrence in the absence of pelvic lymphadenectomy, and 2 had a lung recurrence in the absence of para-aortic lymphadenectomy. The 5-year survival rate was 100% for patients with grade 1 disease and 92% for grade 2 disease. In this single-institution study, the authors concluded that only a small portion of patients would have benefited from routine lymphadenectomy.

Eltabbakh et al[22] evaluated the survival of low-risk endometrial cancer patients without routine lymphadenectomy. Notably, routine vaginal brachytherapy was administered. Over a median of 8.1 years of follow-up, 1.8% of patients died of their disease. Additionally, 2.1% of patients had severe complications from brachytherapy, including severe vaginal stenosis, radiation cystitis, radiation colitis, and rectovaginal fistula.

Hidaka et al[23] compared 68 patients with early-stage disease who underwent complete lymphadenectomy with 60 patients who did not undergo lymphadenectomy. Disease-free survival, overall survival, perioperative complications, and blood transfusions were compared. Overall, there was no significant difference in disease-free and overall survival between the two groups, with a median follow-up of 120 months for the lymphadenectomy cohort and 74 months for the unstaged cohort. However, mean operative time (237 vs 132 minutes), estimated blood loss (771 vs 259 mL), transfusion requirement (23 vs 2 patients), and postoperative leg lymphedema (11 vs 0 patients) were all significantly greater in the lymphadenectomy group. Although this study was not powered to detect differences in survival, it confirmed earlier reports that low-risk patients without complete lymphadenectomy had an excellent prognosis.

In contrast, Kilgore et al[24] found that lymphadenectomy did impact survival. Three groups of endometrial cancer patients were compared retrospectively. One group of 212 patients underwent multiple pelvic node sampling (average of 11 nodes) from at least 4 separate sites. A second group of 205 patients had limited pelvic node sampling (average of 4 nodes) from fewer than 4 sites, and the third group of 208 patients were not sampled. The number of high-risk patients was evenly distributed between the various node sampling groups. The patients who had multiple-site pelvic node sampling had significantly better overall survival than the patients who did not have lymph node sampling ($P = .0002$). Multiple-site pelvic node sampling offered survival benefit in both low-risk and high-risk patients. Additionally, lower recurrence rates were observed in patients with multiple-site pelvic node sampling compared to those patients without node sampling ($P = .019$). This study suggests that the extent of lymph node dissection may be an important consideration when assessing the potential benefits of lymphadenectomy.

A number of other retrospective studies have also suggested a therapeutic benefit for pelvic lymphadenectomy in patients with endometrial cancer.[25-27] Cragun et al[26] reported a survival advantage in patients with early-stage disease with poorly differentiated cancers but failed to demonstrate a similar advantage in grade 1 or 2 disease. In a large, retrospective analysis of over 9,000 women with apparent stage I endometrial cancer, Trimble et al[25] reported that the 5-year relative survival rate for patients who did not undergo lymph node sampling was 98% compared with 96% for patients who had lymph node sampling. Lymph node sampling did not appear to confer a survival benefit in patients with stage IA, grade 1 or 2 tumors, although

improved survival was observed in patients with grade 3 disease who underwent lymph node sampling.

Analyzing patient information from the Surveillance, Epidemiology, and End Results (SEER) program, Chan et al[28] reported on 12,333 endometrial cancer patients who underwent comprehensive surgical staging. This large population was divided into five groups of patients based on the number of lymph nodes resected (1 node, 2–5 nodes, 6–10 nodes, 11–20 nodes, and > 20 nodes). In women with intermediate- or high-risk disease characteristics, a larger number of nodes resected corresponded with improved 5-year survival rates. Furthermore, improved survival with more extensive lymph node resection was seen in women with advanced-stage IIIC–IV cancer. This survival advantage persisted irrespective of the number of nodes positive for disease. However, a survival advantage from lymphadenectomy was not observed in low-risk patients with stage IA (all grades) or stage IB (grades 1 and 2). In a study by Chan et al,[29] surgically staged patients with stage I, grade 3 disease had statistically improved 5-year survival rates compared with unstaged patients (90% vs 85%, $P = .0001$).

One may speculate over which factors account for the greatest impact on survival in this heterogeneous population. Some patients with higher grade and more invasive cancers likely experience a therapeutic benefit from surgical excision of microscopically involved lymph nodes. In many cases, however, the survival difference may be explained by stage migration; specifically, surgically confirmed stage I patients with no lymph node metastasis will have an improved survival compared to clinical stage I patients with undetected disease in the lymph nodes. Selection biases may also influence patient outcomes. Characteristics such as obesity or other comorbidities that affect survival may have influenced the surgeon's decision to perform a lymphadenectomy. In many studies, standardized surgical management protocols and pathologic evaluations were lacking. It is therefore difficult to make definitive conclusions about overall survival from these retrospective studies, and other clinically important factors must be considered when evaluating routine surgical staging.

Morbidity From Lymph Node Dissections and Radiotherapy

It has been argued that the complications from surgical staging may be worse than the side effects of radiotherapy. Morbidity from lymphadenectomy includes lymphedema, symptomatic lymphocyst, deep vein thrombosis, and blood transfusion.[20]

Advocates of routine comprehensive surgical staging have countered that the morbidity from pelvic and para-aortic lymphadenectomy is minimal. In a study comparing 191 surgically staged endometrial cancer patients with 101 non-staged patients, Moore et al[30] did not find significant differences in estimated blood loss, blood transfusions, or vascular injuries between the staged and unstaged groups. There was also no difference in infection rates and length of hospital admission postoperatively. In a prospective trial of 77 patients, Larson et al[31] noted that lymph node sampling resulted in surgeries lasting an average of 40 minutes longer with greater estimated blood loss (approximately 120 mL). There was also a longer average postoperative hospital stay for the surgically staged group. However, lymph node sampling did not result in an increased risk of febrile morbidity, blood transfusion, postoperative complications, or mortality in this study. In general, morbidity from lymphadenectomy is limited if performed by a skilled surgeon.

Morbidity from whole pelvic radiation includes deleterious effects on small and large bowel, urinary bladder, and vaginal function. Adverse gastrointestinal effects are the most common, ranging from mild diarrhea and abdominal cramping to bleeding and obstruction. Urinary bladder complications include dysuria, hematuria, incontinence, fistula, and necrosis. Even relatively mild complications may seriously impact a patient's quality of life. In a retrospective study of 317 patients with endometrial cancer treated with postoperative radiotherapy, late complications were documented in 51%, with 11% of patients suffering from grade 3 or 4 complications.[32] Surgical staging may avoid these potential morbidities by decreasing the utilization of radiotherapy.

Decreasing the Need for Adjuvant Radiation Therapy

There is accumulating evidence that lymphadenectomy decreases the need for whole pelvic radiation in intermediate- and high-risk stage I patients. In a small study of surgically staged high-risk patients treated with only postoperative brachytherapy, Seago et al[33] demonstrated that there were no recurrences with a median of 25 months of follow-up. Lin et al[34] studied 78 surgically staged intermediate-risk patients who were given either adjuvant vaginal brachytherapy or brachytherapy plus whole pelvic radiation. There was no difference in disease-free survival between the two groups. Furthermore, large, multicenter trials such as GOG-99 and the Post Operative Radiation Therapy in Endometrial Carcinoma (PORTEC) study in Europe have suggested that although whole pelvic radiation may decrease local recurrence rates in intermediate-risk endometrial carcinoma, there is no improvement in overall survival.[5,35]

Straughn et al[36] retrospectively studied 239 surgical stage I patient with intermediate-risk factors. Overall survival and recurrences in patients who received adjuvant radiotherapy were compared to patients who were observed. Although recurrence rates were higher in the observation cohort, survival was similar in both

cohorts. The majority of patients who recurred were successfully salvaged with radiotherapy. In a subsequent multi-institution study, Straughn et al[37] compared the outcomes of comprehensively staged IC patients who were treated with adjuvant radiation therapy or observation. This study demonstrated no difference in overall survival between the groups and suggested that fully staged patients with IC endometrial adenocarcinoma may safely forego adjuvant radiation therapy.

These results were confirmed by Goudge et al[10] who showed that surgically staged intermediate-risk patients with negative lymph nodes had similar recurrence rates whether or not they were treated with whole pelvic radiation. These studies underscore the fact that traditional risk factors such as myometrial invasion serve only to estimate the likelihood of extrauterine metastasis. Once extrauterine disease is definitively ruled out by comprehensive staging, the risk of recurrence is generally quite low.

Impact of Surgical Staging on Clinical Care

It has been argued that the information obtained from comprehensive surgical staging significantly impacts postoperative management.[19] In a study of 181 patients with grade 1 disease, Ben-Shachar et al[11] reported that adjuvant treatment was avoided in 17% of patients as a result of negative staging results. The results of surgical staging also led to adjuvant treatment in 12% of patients who were found to have extrauterine disease or other high-risk characteristics. In this study, surgical staging significantly impacted postoperative treatment in a significant number of patients. Therefore, several authors recommend comprehensive surgical staging to be performed on all patients with endometrial cancer, including those with grade 1 disease.[11,18]

The Role of Para-aortic Lymphadenectomy

In an effort to minimize surgical morbidity, studies have been conducted to ascertain the safety and practicality of performing only pelvic lymphadenectomy and eliminating para-aortic sampling from the staging procedure. Reports of morbidity in women receiving pelvic and para-aortic lymphadenectomy compared with pelvic lymphadenectomy alone are conflicting. In one study, patients undergoing both procedures had longer surgeries (median 220 vs 204 minutes), longer hospitalizations (8 vs 5 days), and greater estimated blood loss.[26] However, other studies failed to report a difference in patients who had a para-aortic lymphadenectomy.[31]

In a retrospective study, Faught et al[38] concluded that 88 para-aortic lymphadenectomies would need to be performed to potentially benefit 4 patients and that pelvic lymphadenectomy with peritoneal washings was sufficient to identify patients with extrauterine disease. Hirahatake et al[39] observed that para-aortic lymph node metastases were present in 2.5% of stage IA, 8.5% of stage IB, and 15.7% of stage II endometrial cancers. Again, a relationship was observed between high-risk factors such as deep myometrial invasion, cervical involvement and lymphovascular space invasion, and the presence of lymph node metastasis.

Mariani et al[40] reported that positive pelvic lymph nodes and lymphovascular space invasion were independent predictors of para-aortic lymph node involvement. Para-aortic lymph nodes were positive in 47% of patients who also had disease documented in their pelvic nodes. Tanaka et al[41] also found a strong correlation between pelvic and para-aortic lymph node involvement. Based on these results, patients with positive pelvic nodes or lymphovascular space invasion who did not undergo para-aortic lymphadenectomy should receive adjuvant radiotherapy to the para-aortic lymph nodes.

Another unanswered question is the anatomical extent of para-aortic resection. Traditionally, most surgeons have removed the para-aortic nodes up to the inferior mesenteric artery (IMA).[36,37] However, some recent studies suggest there is a high incidence of positive lymph nodes above the IMA. For example, Mariani et al[42] reported that 77% of patients with para-aortic metastases had involvement above the IMA, while only 40% of the ipsilateral nodes below the IMA were reported positive. Of note, the number of patients with isolated disease above the IMA is quite low, and the majority of patients with disease above the IMA also have disease in the pelvic nodes and low para-aortic nodes.

Economic Considerations: What Is Cost-Effective?

If the various treatment strategies for early-stage endometrial cancer result in similar survival, then quality of life and cost of therapy should be considered. There are many variables to evaluate when identifying the most cost-effective treatment strategy. In addition to estimating the costs of surgery and radiotherapy, accurately quantifying the costs of side effects from surgery, radiation therapy, and other comorbidities remains a challenge.

Studies evaluating the cost-effectiveness of different management strategies in early-stage endometrial cancer have utilized different cost assumptions.[43-47] Barnes et al[43] evaluated routine surgical staging for all patients with adjuvant radiation therapy reserved for patients with extrauterine disease. This strategy was compared to lymph node dissection only for high-risk patients with deep myometrial invasion or intraoperative frozen section with a surgical consultation. The surgical staging strategy was the most cost-effective strategy in this cost analysis. More recently, Cohn et al[47] performed a cost-effectiveness analysis in patients with preoperative grade 1 disease. Three strategies were compared: (1) complete surgical staging in all patients, (2) frozen section followed by selective surgical stag-

ing, and (3) hysterectomy without staging. Based on estimated costs for surgery, chemotherapy, and radiotherapy, the complete surgical staging approach was the most cost-effective, decreased postoperative radiation, and resulted in equivalent survival rates.

Alternative Approaches to Open Lymphadenectomy

In the last 15 years, an increasing number of surgeons have been utilizing a minimally invasive approach to surgically treat endometrial cancer.[48] The benefit of laparoscopic staging over laparotomy in endometrial cancer patients has been well documented. Multiple studies have shown no difference in survival or recurrence between laparoscopy and laparotomy staging, in both early- and advanced-stage endometrial cancer.[49-51] Furthermore, significant improvements in early postoperative complications (23.8% vs 47.4%; $P = .011$) and late postoperative complications (7.9% vs 35.5%; $P = .001$) were demonstrated in a prospective study of 122 endometrial cancer patients.[52] Frigerio et al[53] confirmed that laparoscopic staging yielded comparable lymph node counts (17 vs 19; $P = .294$). Although the laparoscopic approach results in a longer operating time (220 vs 175 minutes; $P < .01$), there was a significantly shorter hospital stay, less blood loss, and fewer postoperative complications in the laparoscopic group. Some authors have reported that the economic benefits from faster recovery are offset by increased anesthesia costs and longer operating room time.[54] Higher hospital costs, longer hospitalizations, higher pharmacy billing, and increased costs related to complications are seen with laparotomy compared to laparoscopy. Furthermore, patients undergoing laparotomy experience a significantly longer time to return to normal activity compared with laparoscopy.[55]

In an effort to decrease the morbidity that results from lymphadenectomy, the sentinel node approach has been successfully employed in other malignancies such as breast and vulvar cancers. The sentinel node is the first node that receives lymphatic drainage in the lymphatic chain. If the sentinel node is pathologically negative, all downstream nodes should also be negative and would not require resection.

Various methods to identify the sentinel node have been utilized such as injecting an isosulfan blue dye, using a radioactive gamma probe, or combining the two techniques. Burke et al[56] utilized isosulfan blue dye at the time of exploratory laparotomy, injecting into the uterine subserosa in 15 high-risk patients. Dye uptake was noted in 67% of cases. In this study, 4 patients had tumor in resected lymph nodes, with only 2 containing blue dye. In a subsequent study combining blue dye with technetium-99 radiocolloid, a sentinel lymph node was identified in only 8 of 18 patients (45%).[57]

Using a hysteroscope to direct dye injection, Niikura et al[58] injected radioactive 99m-technetium (^{99m}Tc) phytate with blue dye in 28 patients with endometrial cancer. The following day, a lymphoscintigram was taken just prior to surgery. A gamma-probe was then used intraoperatively, and all radioactive nodes were removed. This technique yielded an overall detection rate of 82%. Of 6 patients with deep myometrial invasion, only 2 were identified, possibly due to altered lymphatic drainage.[58] Delaloye et al[59] also used a hysteroscope to guide lymphatic mapping and found a positive sentinel node in 8 of 9 patients (89%) with metastatic disease. There may be an increased role for sentinel lymph node biopsy in endometrial cancer in the future, but presently this is still an investigational technique.

Conclusions

Multiple studies have demonstrated benefits from comprehensive surgical staging in patients with endometrial cancer. Preoperative studies, including PET/CT, MRI, and dilation and curettage are not accurate methods to evaluate the lymph nodes. Likewise, intraoperative assessments such as lymph node palpation and frozen section have been shown to be inadequate. Subjecting patients with an excellent overall prognosis to comprehensive surgical staging to identify a small number of patients with more advanced disease has been controversial. Weighing the morbidity of lymphadenectomy against the morbidity of adjuvant radiation therapy requires careful clinical judgment. It appears that comprehensive surgical staging allows the surgeon to identify high-risk endometrial cancer patients who would benefit from adjuvant therapies. Adjuvant radiation therapy has drastically decreased during the last decade due to the increase utilization of lymphadenectomy. The morbidity from lymphadenectomy appears to be reduced with the use of laparoscopic staging, with similar nodal counts and survival outcomes.

Disclosures

No significant relationship exists between the authors and the companies/organizations whose products or services may be referenced in this article.

References

1. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2008. *CA Cancer J Clin.* 2008;58(2):71-96. Epub 2008 Feb 20.
2. Ries LAG, Young JL, Keel GE, et al. SEER Survival Monograph: Cancer Survival Among Adults: US SEER Program, 1988-2001, Patient and Tumor Characteristics. National Cancer Institute, SEER Program, NIH Pub. No. 07-6215, Bethesda, MD, 2007.
3. Creasman WT, Morrow CP, Bundy BN, et al. Surgical pathologic spread patterns of endometrial cancer: a Gynecologic Oncology Group study. *Cancer.* 1987;60(8 suppl):2035-2041.
4. Takeshima N, Hirai Y, Tanaka N, et al. Pelvic lymph node metastasis in endometrial cancer with no myometrial invasion. *Obstet Gynecol.* 1996; 88(2): 280-282.
5. Keys HM, Roberts JA, Brunetto VL, et al. A phase III trial of surgery with or without adjunctive external pelvic radiation therapy in intermediate risk endometrial adenocarcinoma: a Gynecologic Oncology Group study. *Gynecol Oncol.* 2004;92(3):744-751.
6. Havrilesky LJ, Cragun JM, Calingaert B, et al. Resection of lymph node metastases influences survival in stage IIIC endometrial cancer. *Gynecol*

Oncol. 2005;99(3):689-695. Epub 2005 Aug 29.

7. Fujimoto T, Nanjyo H, Nakamura A, et al. Para-aortic lymphadenectomy may improve disease-related survival in patients with multipositive pelvic lymph node stage IIIc endometrial cancer. *Gynecol Oncol*. 2007;107(2):253-259. Epub 2007 Jul 19.

8. Gehrig PA, Groben PA, Fowler WC Jr, et al. Noninvasive papillary serous carcinoma of the endometrium. *Obstet Gynecol*. 2001;97(1):153-157.

9. Chan JK, Loizzi V, Youssef M, et al. Significance of comprehensive surgical staging in noninvasive papillary serous carcinoma of the endometrium. *Gynecol Oncol*. 2003;90(1):181-185.

10. Goudge C, Bernhard S, Cloven NG, et al. The impact of complete surgical staging on adjuvant treatment decisions in endometrial cancer. *Gynecol Oncol*. 2004;93(2):536-539.

11. Ben-Shachar I, Pavelka J, Cohn DE, et al. Surgical staging for patients presenting with grade 1 endometrial carcinoma. *Obstet Gynecol*. 2005;105(3): 487-493.

12. Zerbe MJ, Bristow R, Grumbine FC, et al. Inability of preoperative computed tomography scans to accurately predict the extent of myometrial invasion and extracorporal spread in endometrial cancer. *Gynecol Oncol*. 2000;78(1): 67-70.

13. Hricak H, Rubinstein LV, Gherman GM, et al. MR imaging evaluation of endometrial carcinoma: results of an NCI cooperative study. *Radiology*. 1991; 179(3):829-832.

14. Park JY, Kim EN, Kim DY, et al. Comparison of the validity of magnetic resonance imaging and positron emission tomography/computed tomography in the preoperative evaluation of patients with uterine corpus cancer. *Gynecol Oncol*. 2008;108(3):486-492. Epub 2008 Jan 16.

15. Girardi F, Petru E, Heydarfadai M, et al. Pelvic lymphadenectomy in the surgical treatment of endometrial cancer. *Gynecol Oncol*. 1993;49(2):177-180.

16. Arango HA, Hoffman MS, Roberts WS, et al. Accuracy of lymph node palpation to determine the need for lymphadenectomy in gynecologic malignancies. *Obstet Gynecol*. 2000;95(4):553-556.

17. Eltabbakh GH. Intraoperative clinical evaluation of lymph nodes in women with gynecologic cancer. *Am J Obstet Gynecol*. 2001;184(6):1177-1181.

18. Case AS, Roconni RP, Straughn JM Jr, et al. A prospective blinded evaluation of the accuracy of frozen section for the surgical management of endometrial cancer. *Obstet Gynecol*. 2006;108(6):1375-1379.

19. Orr JW Jr, Naumann WR, Escobar P. "Attitude is a little thing that makes a big difference" Winston Churchill. *Gynecol Oncol*. 2008;109(1):147-151; author reply 151-153. Epub 2008 Feb 19.

20. Aalders JG, Thomas G. Endometrial cancer: revisiting the importance of pelvic and para aortic lymph nodes. *Gynecol Oncol*. 2007;104(1):222-231. Epub 2006 Nov 28.

21. Belinson JL, Lee KR, Badger GJ, et al. Clinical stage I adenocarcinoma of the endometrium: analysis of recurrences and the potential benefit of staging lymphadenectomy. *Gynecol Oncol*. 1992;44(1):17-23.

22. Eltabbakh GH, Piver MS, Hempling RE, et al. Excellent long-term survival and absence of vaginal recurrences in 332 patients with low-risk stage I endometrial adenocarcinoma treated with hysterectomy and vaginal brachytherapy without formal staging lymph node sampling: report of a prospective trial. *Int J Radiat Oncol Biol Phys*. 1997;38(2):373-380.

23. Hidaka T, Kato K, Yonezawa R, et al. Omission of lymphadenectomy is possible for low-risk corpus cancer. *Eur J Surg Oncol*. 2007;33(1):86-90. Epub 2006 Nov 13.

24. Kilgore LC, Partridge EE, Alvarez RD, et al. Adenocarcinoma of the endometrium: survival comparisons of patients with and without pelvic node sampling. *Gynecol Oncol*. 1995;56(1):29-33.

25. Trimble EL, Kosary C, Park RC. Lymph node sampling and survival in endometrial cancer. *Gynecol Oncol*. 1998;71(3):340-343.

26. Cragun JM, Havrilesky LJ, Calingaert B, et al. Retrospective analysis of selective lymphadenectomy in apparent early-stage endometrial cancer. *J Clin Oncol*. 2005;23(16):3668-3675. Epub 2005 Feb 28.

27. Mohan DS, Samuels MA, Selim MA, et al. Long-term outcomes of therapeutic pelvic lymphadenectomy for stage I endometrial adenocarcinoma. *Gynecol Oncol*. 1998;70(2):165-171.

28. Chan JK, Cheung MK, Huh WK, et al. Therapeutic role of lymph node resection in endometroid corpus cancer: a study of 12,333 patients. *Cancer*. 2006;107(8):1823-1830.

29. Chan JK, Wu H, Cheung MK, et al. The outcomes of 27,063 women with unstaged endometrioid uterine cancer. *Gynecol Oncol*. 2007;106(2): 282-288.

30. Moore DH, Fowler WC Jr, Walton LA, et al. Morbidity of lymph node sampling in cancers of the uterine corpus and cervix. *Obstet Gynecol*. 1989; 74(2):180-184.

31. Larson DM, Johnson K, Olson KA. Pelvic and para-aortic lymphadenectomy for surgical staging of endometrial cancer: morbidity and mortality. *Obstet Gynecol*. 1992;79(6):998-1001.

32. Jereczek-Fossa B, Jassem J, Nowak R, et al. Late complications after postoperative radiotherapy in endometrial cancer: analysis of 317 consecutive cases with application of linear-quadratic model. *Int J Radiat Oncol Biol Phys*. 1998;41(2):329-338.

33. Seago DP, Raman A, Lele S. Potential benefit of lymphadenectomy for the treatment of node-negative locally advanced uterine cancers. *Gynecol Oncol*. 2001;83(2):282-285.

34. Lin LL, Mutch DG, Rader JS, et al. External radiotherapy versus vaginal brachytherapy for patients with intermediate risk endometrial cancer. *Gynecol Oncol*. 2007;106(1):215-220. Epub 2007 May 7.

35. Creutzberg CL, van Putten WL, Koper PC, et al. Surgery and postoperative radiotherapy versus surgery alone for patients with stage-1 endometrial carcinoma: multicentre randomised trial. PORTEC Study Group. Post Operative Radiation Therapy in Endometrial Carcinoma. *Lancet*. 2000; 355(9213): 1404-1411.

36. Straughn JM, Huh WK, Kelly FJ, et al. Conservative management of stage I endometrial carcinoma after surgical staging. *Gynecol Oncol*. 2002; 84(2):194-200.

37. Straughn JM, Huh WK, Orr JW Jr, et al. Stage IC adenocarcinoma of the endometrium: survival comparisons of surgically staged patients with and without adjuvant radiation therapy. *Gynecol Oncol*. 2003;89(2):295-300.

38. Faught W, Krepart GV, Lotocki R, et al. Should selective paraaortic lymphadenectomy be part of surgical staging for endometrial cancer? *Gynecol Oncol*. 1994;55(1):51-55.

39. Hirahatake K, Hareyama H, Sakuragi N, et al. A clinical and pathologic study on para-aortic lymph node metastasis in endometrial carcinoma. *J Surg Oncol*. 1997;65(2):82-87.

40. Mariani A, Keeney GL, Aletti G, et al. Endometrial carcinoma: paraaortic dissemination. *Gynecol Oncol*. 2004;92(3):833-838.

41. Tanaka H, Sato H, Miura H, et al. Can we omit para-aorta lymph node dissection in endometrial cancer? *Jpn J Clin Oncol*. 2006;36(9):578-581. Epub 2006 Jul 26.

42. Mariani A, Dowdy SC, Cliby WA, et al. Prospective assessment of lymphatic dissemination in endometrial cancer: a paradigm shift in surgical staging. *Gynecol Oncol*. 2008;109(1):11-18. Epub 2008 Mar 4.

43. Barnes MN, Roland PY, Straughn M, et al. A comparison of treatment strategies for endometrial adenocarcinoma: analysis of financial impact. *Gynecol Oncol*. 1999;74(3):443-447.

44. Orr JW Jr, Holimon JL, Orr PF. Stage I corpus cancer: is teletherapy necessary? *Am J obstet Gynecol*. 1997;176(4):777-788; discussion 788-789.

45. Fanning J, Hofman ML, Andrews SJ, et al. Cost-effectiveness analysis of the treatment for intermediate risk endometrial cancer: postoperative brachytherapy vs observation. *Gynecol Oncol*. 2004;93(3):632-636.

46. Lachance JA, Stukenborg GJ, Schneider BF, et al. A cost-effective analysis of adjuvant therapies for the treatment of stage I endometrial adenocarcinoma. *Gynecol Oncol*. 2008;108(1):77-83. Epub 2007 Oct 22.

47. Cohn DE, Huh WK, Fowler JM, et al. Cost-effectiveness analysis of strategies for the surgical management of grade 1 endometrial adenocarcinoma. *Obstet Gynecol*. 2007;109(6):1388-1395.

48. Barakat RR, Lev G, Hummer AJ, et al. Twelve-year experience in the management of endometrial cancer: a change in surgical and postoperative radiation approaches. *Gynecol Oncol*. 2007;105(1):150-156. Epub 2007 Jan 2.

49. Eltabbakh GH. Analysis of survival after laparoscopy in women with endometrial carcinoma. *Cancer*. 2002;95(9):1894-1901.

50. Holub Z, Jabor A, Bartos P, et al. Laparoscopic surgery for endometrial cancer: long-term results of a multicentric study. *Eur J Gynaecol Oncol*. 2002;23(4):305-310.

51. Nezhat F, Yadav J, Rahaman J, et al. Analysis of survival after laparoscopic management of endometrial cancer. *J Minim Invasive Gynecol*. 2008; 15(2):181-187.

52. Tozzi R, Malur S, Koehler C, et al. Analysis of morbidity in patients with endometrial cancer: is there a commitment to offer laparoscopy? *Gynecol Oncol*. 2005;97(1):4-9.

53. Frigerio L, Gallo A, Ghezzi F, et al. Laparoscopic-assisted vaginal hysterectomy versus abdominal hysterectomy in endometrial cancer. *Int J Gynaecol Obstet*. 2006;93(3):209-213. Epub 2006 Mar 6.

54. Scribner DR Jr, Mannel RS, Walker JL, et al. Cost analysis of laparoscopy versus laparotomy for early endometrial cancer. *Gynecol Oncol*. 1999;75(3):460-463.

55. Spirtos NM, Schlaerth JB, Gross GM, et al. Cost and quality-of-life analyses of surgery for early endometrial cancer: laparotomy versus laparoscopy. *Am J Obstet Gynecol*. 1996;174(6):1795-1799; discussion 1799-1800.

56. Burke TW, Levenback C, Tornos C, et al. Intraabdominal lymphatic mapping to direct selective pelvic and paraaortic lymphadenectomy in women with high-risk endometrial cancer: results of a pilot study. *Gynecol Oncol*. 1996;62(2): 169-173.

57. Frumovitz M, Bodurka DC, Broaddus RR, et al. Lymphatic mapping and sentinel node biopsy in women with high-risk endometrial cancer. *Gynecol Oncol*. 2007;104(1):100-103. Epub 2006 Sep 11.

58. Niikura H, Okamura C, Utsunomiya H, et al. Sentinel lymph node detection in patients with endometrial cancer. *Gynecol Oncol*. 2004;92(2):669-674.

59. Delaloye JF, Pampallona S, Chardonnens E, et al. Intraoperative lymphatic mapping and sentinel node biopsy using hysteroscopy in patients with endometrial cancer. *Gynecol Oncol*. 2007;106(1):89-93. Epub 2007 Apr 17.