Commentary (Moller): Surgical Staging in Endometrial Cancer

January 01, 2006
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Endometrial cancer is the most common gynecologic malignancy affecting women in the United States. In 1988, the International Federation of Gynecology and Obstetrics shifted from a clinical staging protocol to one based on surgical factors, making surgical staging the accepted treatment approach to endometrial cancers, with excellent survival compared to other gynecologic malignancies. The manuscript by Kirby et al brings to light the controversies surrounding the surgical evaluation of endometrial cancers. Although surgical staging has been shown to have both prognostic and therapeutic benefit, major problems in the United States continue to result in suboptimal treatment of patients with endometrial cancer. These problems include the lack of an accepted surgical protocol (in terms of adequacy of lymph node sampling) and incomplete surgical staging secondary to patient factors or the lack of referral to specialty-trained gynecologic oncologists.

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Radiographic assistance in determining preoperative disease extent in patients with endometrial cancers has been shown to be of limited value. Sonographic measurement of endometrial thickness has not been shown to correlate well with tumor grade or stage at final surgery.[1] Other imaging techniques such as computed tomography (CT) or magnetic resonance imaging (MRI) have been shown to predict local-regional staging but remain limited when used to predict lymph node involvement and, therefore, are not useful when predicting extent of indicated surgery.[2] F-18-fluorodeoxyglucose-positron-emission tomography (FDG-PET) also has been shown to have only moderate sensitivity in predicting lymph node metastases preoperatively in women with endometrial cancer.[3] As emphasized by Kirby et al, these modalities should not replace lymphadenectomy but may be helpful in patients where lymphadenectomy cannot be adequately performed or was not performed during the initial surgery. Kirby et al discuss the limited value and potential adverse effects of adding hysteroscopy to traditional endometrial sampling techniques. Given that the procedure increases cost and potential surgical morbidities, as well as some evidence that suggests a higher incidence of positive peritoneal cytology, hysteroscopy is not endorsed as a significant addition to the preoperative evaluation in patients with abnormal bleeding. Other authors have attempted to correlate phenotypic and molecular markers (ploidy, proliferating cell nuclear antigen, p53, HER2/neu, bcl-2, estrogen receptor, progesterone receptor) in preoperative endometrial samples with morphologic data and disease stage at hysterectomy in an attempt to better identify patients at risk of lymph node metastases.[4] Larger studies need to be performed to fully assess the clinical utility of these potential associations before dictating surgical management decisions. The majority patients will still benefit from complete surgical staging where indicated. **Staging Procedure**

Kirby et al remind us that the decision to perform comprehensive surgical staging should ideally be made prior to entering the operating room. Significant data highlight the limitations of using preoperative tumor grade, cell type, and depth of myometrial invasion to assess risk of lymph node metastases.[5] As Kirby et al review, many of these intraoperative algorithms become less accurate as tumor grade increases, and they are significantly limited by the experience of the surgeon and reading pathologist. Advocates for the use of intraoperative algorithms to dictate extent of surgical
dissection refer to the idea that increased surgical dissection equals increased surgical morbidity. Available data, however, suggest that when performed by a trained, experienced surgeon, hysterectomy and lymph node dissections can be performed safely with minimal or no increase in morbidity as measured by blood loss, operative time, infections, thromboembolic phenomena, and hospital stay, as detailed by Kirby et al.[6-7] As Kirby et al report, several studies have demonstrated that a laparoscopy-assisted staging procedure can be safely performed in these patients and is associated with shorter hospital stays and blood loss despite higher operative costs. What is important to highlight, however, is the quality-of-life benefit of laparoscopic staging, including shorter time to return to normal activity and potentially shorter time to commence adjuvant radiation therapy if indicated. Problems such as port site recurrences and the surgeon's lack of education or experience with the laparoscopic technique need to be further addressed.

Benefits of Surgical Staging

Kirby et al note that women undergoing definitive surgery for endometrial cancer should undergo thorough surgical staging, even when low-grade disease is found on preoperative biopsy, irrespective of gross or frozen assessment of depth of myometrial invasion. Up to 30% of grade I cancers will demonstrate postoperative histologic factors that highlight the need for surgical staging to address whether adjuvant radiation therapy would be of benefit.[8] If patients are adequately staged, surgical documentation of lack of extrauterine disease can allow selected patients to forgo costly and potentially morbid adjuvant radiation therapy. As Kirby et al point out, the recent report from the Gynecologic Oncology Group on adjuvant radiation therapy in intermediate-risk, early-stage endometrial cancer patients did show a decreased risk of pelvic recurrence. However, this result came at the price of increased complications, and overall survival was not improved. Other authors highlight the need for further study about the role of adjuvant radiation therapy for intermediate-risk endometrial cancer. The definition of who is truly at high risk and who would benefit from adjuvant therapy as well as the comparison of potentially less morbid radiation techniques (such as vaginal brachytherapy) in this group of patients needs to be better delineated in larger studies.[9] If the true surgical stage is not known, the interpretation of survival impact for these different patient categories and adjuvant modalities becomes difficult if not impossible.

Conclusions

Kirby et al highlight the importance of adequate surgical staging in endometrial cancer patients and the clinical and economic impact the process can have on the treatment of this generally curable disease. Patients managed by gynecologic oncologists are more likely to undergo comprehensive staging and are, therefore, less likely to receive potentially morbid radiation therapy. Emphasizing public education regarding the benefits of having an adequate surgical procedure as well as professional education regarding the need for subspecialty referral will hopefully continue to improve the delivery of gynecologic care to women facing endometrial cancer in the United States.

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Disclosures:
The author has no significant financial interest or other relationship with the manufacturers of any products or providers of any service mentioned in this article.

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