Changing Concepts in the Management of Endometrial Cancer

Review Article [1] | July 01, 1996
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The authors present the major issues and controversies surrounding the treatment of endometrial cancer. A variety of therapeutic approaches have been used in the past, including surgery alone, preoperative radiation and surgery, surgery and postoperative radiation, radiation alone for medically inoperable patients, and surgery with pelvic, whole-abdominal and/or vaginal cuff irradiation. Many of the series justifying these different modalities were based on clinical staging. As the authors point out, the Gynecologic Oncology Group (GOG) finally provided the pathologic data that resulted in a reassessment of the treatment of endometrial cancer [1-3]. This led to the 1988 consensus by the International Federation of Gynecology and Obstetrics (FIGO), which paved the way for surgical staging of all but inoperable patients. However, as the authors appropriately note, there is still no agreement as to which patients need nodal sampling. This development set the stage for studies readdressing the issue of adjuvant therapy. Although numerous reports of both retrospective and prospective data have attempted to answer the question of who needs additional treatment [4-9], few prospective randomized trials are available. To its credit, the GOG has been instrumental in attempting to answer this very question.

Controversies in Early-Stage Disease

Two recent papers highlight the controversies in early-stage disease. The first report from Denmark divided patients into pathologic stage I (P-I) low-risk, P-I high-risk, P-II, and P-III. In 1986, the Danish Endometrial Cancer Group decided not to offer adjuvant postoperative treatment to the P-I low-risk group, while recommending pelvic external irradiation for the remaining groups [10]. Of the total of 1,214 patients, 641 fell into the P-I low-risk group (grades 1 and 2 with equal to or more than 50% myometrial invasion) and suffered only a 7% recurrence rate at 68 to 92 months' follow-up. The P-I high-risk, P-II, and P-III patients had recurrence rates of 15%, 29%, and 47%, respectively. Additional treatment salvaged 15 of 17 vaginal recurrences.

A study by Ackerman et al [11] used the existence of a similarly effective treatment of recurrent disease as one argument against routine adjuvant pelvic irradiation for early-stage endometrial cancer. There is no question that there is a group of endometrial cancer patients whose prognosis is so favorable that they do not need additional treatment. The uncertainty has revolved around the definition of how good is good enough.

GOG protocol #99 addresses the issue of whether intermediate-risk (grades 1, 2, 3; stages IB, IC, IIA [occult], IIB [occult]) patients would benefit from postoperative pelvic irradiation. A total of 396 evaluable patients are currently undergoing statistical analysis (J.A. Roberts, md, personal communication, 1996). However, most of the enrolled patients have low-risk parameters, so that it may not be possible for this study to answer the question of whether higher-risk patients benefit from postoperative radiotherapy.

When to Use Chemotherapy?

Karasek and Faul also discuss the controversy surrounding the use of systemic chemotherapy in endometrial cancer. Should chemotherapy be used in lieu of radiotherapy or in combination with it? Again, the GOG is attempting to resolve this issue by conducting several current trials.

The GOG study #156 is a randomized trial of postoperative pelvic radiation vs doxorubicin plus cisplatin (Platinol) in patients with stage IB, IC, IIA, or IIB high-risk endometrial cancer (T.W. Burke, md, personal communication, 1996). These patients must have two or more of the following characteristics: grade 3, clear cell or papillary serous histology, greater than one-third myometrial invasion, and vascular space invasion. This study began in July 1995; thus, it will take some time before this question is answered.

The use of systemic chemotherapy vs pelvic or whole-abdominal radiation for advanced stage III/IV...
endometrial cancer continues to be a topic of discussion among both gynecologic and radiation oncologists. In response to this, in 1992 the GOG launched a prospective, randomized, phase III trial (GOG #122) of whole-abdominal radiotherapy vs the combination of doxorubicin and cisplatin chemotherapy in stage III/IV endometrial cancer. As of January 1996, 120 patients were evaluable, and the trial is continuing to accrue patients (M.E. Randall, md, personal communication, January 1996).

Potential Benefit of Vaginal Cuff Irradiation

Karasek and Faul also touch on the possible benefit of vaginal cuff treatment as either the sole method of treatment or in conjunction with pelvic radiation (as it is frequently used in the community). Clearly, this area is ripe for a prospective, randomized trial. In addition to optimal adjuvant therapy, the authors discuss appropriate follow-up, which, in today's era of cost containment, has become an increasingly important issue. Those concerned with endometrial cancer are by no means the only ones attempting to grapple with this problem [12]. The cost-benefit ratio for various follow-up assessments requires careful analysis. Accurate information is needed on the frequency, cost, and preventability of various outcomes. That kind of data is currently lacking in national cooperative group trials.

As evidenced by a recent article by Corn and Rubin entitled, "Should Treatment of High Risk Endometrial Cancer Include Postoperative Radiotherapy?" [13], the postoperative adjuvant management of endometrial cancer continues to be controversial.

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