Our cancer center championed the A Study in the Treatment of Endometrial Cancer (ASTEC) trial,1 topping the patient recruitment league table. However, we continue to perform lymphadenectomy surgical staging for potential high-and/or intermediate-risk histologic cases. The appropriateness of lymphadenectomy cannot be divorced from adjuvant therapy algorithm. We do not administer adjuvant radiotherapy for confirmed node-negative intermediate-risk cases. Conversely, our guidelines advise pelvic radiotherapy for high- and/or intermediate-risk histologic cases where lymphadenectomy has been omitted because of the presumed higher risk of pelvic sidewall recurrence from occult pelvic nodal disease.

Although adjuvant external beam pelvic radiotherapy reduces the risk of pelvic recurrence, the meta-analysis of PORTEC, ASTEC + EN.5 and GOOG99 confirms that it does not improve survival.2,3 However, external beam radiotherapy causes potential morbidity: acute toxicity incidence, 57% versus 27% (ASTEC); late toxicity, 61% versus 45% (ASTEC); and late complications, 25% versus 6% (PORTEC). Radiotherapy is also associated with an increased relative risk of 40% of a second neoplasm at 10 years4 and has a negative impact on the quality of life for long-term survivors.5 Conversely, ASTEC also demonstrates morbidity from lymphadenectomy, particularly moderate/severe lymphedema (0.341% vs 0.003%). If one intervention could safely obviate the need for the other, the question is which intervention is likely to cause less debilitating morbidity or harm fewer patients.

In ASTEC, high- and/or intermediate-risk histologic cases underwent second randomization to avoid differences in postsurgical treatment on the basis of nodal histology, any differences being attributed to lymphadenectomy. The frustrating consequence is that we cannot assess the clinically relevant comparison between high- and/or intermediate-risk node-negative lymphadenectomy without adjuvant therapy and conventional surgery with adjuvant radiotherapy.

GOOG99 randomized external beam radiotherapy without brachytherapy for intermediate-risk node-negative lymphadenectomy patients. The major difference was the number of vaginal vault recurrences; local recurrence 1.6% radiotherapy versus 7.4% no adjuvant therapy at 2 years. Confirming other trials, there was no survival difference, but the radiotherapy arm reported more frequent and severe toxicities. Vaginal vault recurrences in nonirradiated patients are potentially salvageable with radiotherapy. However, the effectiveness of adjuvant brachytherapy is also high, PORTEC-2 showing a 0.9% vaginal recurrence rate with low morbidity,1 compared with 19% for a similar cohort without adjuvant treatment in PORTEC. Perhaps lymphadenectomy surgical staging of intermediate-risk cases with adjuvant brachytherapy for node-negative patients may achieve pelvic disease control with minimal morbidity.

Women continue to die from distant metastatic disease, particularly associated with high-risk histology. Among conventional treatment modalities, only adjuvant chemotherapy offers hope to prevent distant recurrence. PORTEC 3 will assess the benefit of chemotherapy with radiotherapy for incompletely staged high- and/or intermediate-risk disease, with adjuvant radiotherapy as the control arm. Perhaps, we should evaluate brachytherapy and chemotherapy without external beam radiotherapy for lymphadenectomy-staged node-negative patients at lower risk of pelvic sidewall recurrence.

Guidelines should consider the efficacy and morbidity of the complete treatment pathway. Despite the findings of ASTEC, there is arguably a role for lymphadenectomy to assist in triage of patients for adjuvant therapy to minimize the risk of treatment-related morbidity without compromising overall survival.

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