Commentary (Kavanagh): Sentinel Node Evaluation in Gynecologic Cancer

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By a long-standing strategy, practitioners have sought to lessen the morbidity associated with the treatment of pelvic malignancies. With careful understanding of pathologic prognostic factors and the natural histories of recurrence and metastatic disease, as well as improvement of imaging studies, there has been a significant reduction in the radicality of gynecologic surgery.[1-3]

Importance of Lymph Node Status

It is generally accepted that lymph node status is one of the most important prognostic factors in vulvar and cervical carcinoma.[4,5] The problematic area has remained the long-standing practice of evaluating lymph node status by complete or near-complete lymph node resections followed by pathologic evaluation. It is clear that extensive lymph node dissection adds to morbidity and increases the complications of radiation therapy.[6-10]

Because anatomists have felt that lymph node drainage is predictable but not uniform, identification of the "first leve" lymph node as the gatekeeper or indicator of subsequent metastatic disease would be most useful. This concept has led to the term "sentinel node," which was first applied in the setting of penile cancer, as identified by lymphangiogram.[11] Such a node would enable us to predict the probability of metastatic disease beyond that node. This is assumed to be information of adequate independent prognostic value to alter effective subsequent therapies.

The review of sentinel node evaluation in gynecologic cancer by Marie Plant et al provides a well-balanced and cautious overview of this technology. Indeed, it is difficult to be very critical of this paper when the concluding statements call for more data before these techniques can become a standard of care. The focus of my discussion will be more on emphasizing the unresolved issues of sentinel node evaluation.

Statistical Weakness

The primary unresolved issue involving sentinel node evaluation is the statistical weakness of the studies. The number of patients entered into each study is relatively small, and thus the authors are required to provide summary tables based on retrospective literature review. These tables represent combinations of different techniques-blue dye, pre- or intraoperative radioscintigraphy, either alone or combination-and the success rates of sentinel lymph node detection and negative predictive values. The summary of the studies increases the rate of sentinel node detection but markedly compromises interstudy comparisons. Furthermore, the authors' tables include data on laparotomy and laparoscopy; the latter approach has gained more popularity in recent years but remains to be proven.

Another important issue is that most studies include patients who are studied during the surgeon's early phase of the "learning curve"; this factor certainly affects the procedure's overall success rate. Indeed, the recent work of these authors and their colleagues on laparoscopic sentinel node mapping in cervical cancer-involving the largest population studied to date-clearly demonstrated the significance of the learning curve on the success of the procedure.[12]

In addition, most of the studies have a very short follow-up period with no subsequent reporting on recurrence or outcome, which may reflect the presence of micrometastasis or unrevealed distant metastasis beyond this node. In the absence of multicenter prospective trials utilizing a uniform technique and accounting for operator experience, one can only look at the data as a weak
meta-analysis. We look forward to the result of the Gynecologic Oncology Group trial (GOG 173) currently being conducted on the sentinel node approach in vulvar cancer.

Lack of Consensus

A second issue is that of the required multidisciplinary nature of this approach. Aside from initial experience with finding the sentinel node, there must be agreement by surgical colleges as to what constitutes an adequate sentinel node evaluation, agreement among pathologists as to the management of the sentinel lymph node (including the number of frozen sections and whether molecular marker evaluations are used), and the format of patient databases, allowing long-term and adequate follow-up. I am not aware of a nationally or internationally agreed-upon manual or guidelines for such a diagnostic or data management approach.

Third, what is the clinical significance of micrometastatic disease (and its treatment)? It is questionable whether a single micrometastatic focus in the sentinel node implies poor prognosis and increased mortality; this issue is even unresolved in breast cancer, for which the sentinel node concept has long been applied.[13] Early data in sentinel lymph node biopsy in breast cancer suggest no adverse outcome for patients with micrometastases.[14] One cannot eliminate the concept and the existence of a host relationship with microscopic residual cancer that does not have a longterm significant morbidity or mortality. Indeed, this has been learned in the setting of malignant melanoma, where the prognosis of patients with micrometastases is significantly better than that for patients with macrometastases.[15] The issue becomes even more pertinent if molecular marker techniques identify metastatic disease in the lymph node at the single-cell level.

Fourth, there is an assumption that the decreased morbidity of the lymph node resection will translate to a positive psychosocial benefit, ie, producing less impact on quality of life, fewer chronic morbidities, and specific improvements in function. At the moment, this benefit must be considered pure speculation. Focused evaluations of sexual function, fatigue, and longterm benefit to the patient are absent. It remains to be proved that limiting lymph node sampling will markedly modify therapy based on other prognostic factors and lead to extended general psychosocial advantage.

Technologic Issues

Fifth, sentinel node evaluation may need to compete with emerging technologies. However, other imaging studies have had a greater role in evaluating disease and lymph node status in more advanced disease. For example, positron-emission tomography (PET) has a provocative role in evaluating nodal status in vulvar and cervical cancer.[16,17] The increasing use of magnetic resonance imaging with newer imaging aspects may provide further prognostic factors that determine disease status (including lymph node status) and subsequent therapies.[18] The combination of PET and computerized tomography may provide information that makes the identification of a sentinel node more contributory to the management of only early-stage disease. One should also not ignore the evaluation of molecular markers on the primary lesion as being a powerful prognostic factor.

Sixth, is a decision regarding whether the blue dye technique or radiolabeled lymphoscintigraphy should be the preferred technology. It is difficult to imagine that there will be a generalized use of these techniques in the absence of a decision on a uniform diagnostic approach.

Final Considerations

Seventh, the current health-care environment will require an analysis of the cost-effectiveness of such work. Clearly, sentinel node evaluation requires additional time, modification of pathology technique, and training of physicians. What is the impact on overall resource utilization? Is this technology worth the investment?

The authors have provided an excellent, detailed, and fair overview of sentinel lymph node methodologies in gynecologic cancer. Indeed, the paper raises more questions than answers.

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