Commentary (Thigpen): The Management of Early Ovarian Cancer

February 01, 1995
By J. Tate Thigpen, MD [1]

Schilder and colleagues have provided a detailed and excellent review of the management of early ovarian carcinoma. Several areas of the review deserve comment and will be considered in the following order: staging and prognostic factors, conservative surgery, and adjuvant therapy.

Staging and Prognostic Factors
With regard to staging and prognostic factors, the review appropriately emphasizes the importance of surgical staging to the decision-making process in stage I and II ovarian carcinoma. The current standard of care, which will be discussed in more detail subsequently, recommends surgery-only for patients at low risk for recurrence, adjuvant therapy for those at high risk, and a more complex sequence of chemotherapy and reexploration for those with advanced disease. A proper and detailed staging laparotomy is mandatory, therefore, before decisions are made about the approach to a particular patient. This entails a repeat laparotomy prior to treatment decisions in those patients who have had inadequate initial operations.

After an adequate staging laparotomy establishes that the patient truly has completely resected stage I or II disease, the physician must assign the patient to either a low-risk or high-risk category. The problem is determining what characteristics establish risk most reliably. Although the cited studies yield differing results, certain factors are identified as significant in virtually all reports: grade 3 differentiation, clear cell histology, large-volume ascites, and aneuploidy. Other factors identified in specific studies include: capsular rupture, tumor excrescences on the surface of the ovary, extra-ovarian spread, positive peritoneal cytology, dense adherence, and certain morphometric parameters. Until future trials clarify the relative importance of these additional factors, it is reasonable to consider the presence of any one of these ten features as indicative of a high risk for recurrence.

Caveats Regarding Conservative Surgery
With regard to surgical therapy, the review indicates that conservative therapy consisting of unilateral salpingo-oophorectomy is an acceptable alternative in younger patients who wish to preserve childbearing function. It is important, however, to emphasize two considerations. First, conservative surgery is not appropriate for patients who are at high risk for recurrence. Secondly, two of the three references cited by the review show compromised survival for patients treated with conservative surgery. The patient must clearly understand the possibility of compromised survival before such a choice is made.

Adjuvant Therapy
With regard to adjuvant therapy, virtually all studies show that, in carefully staged patients, those at low risk for recurrence have a 5-year disease-free survival rate that exceeds 90% with surgical resection alone. In contrast, in high-risk patients, data from the Italian Interregional Cooperative Group of Gynecologic Oncology cited in the review suggest that 5-year disease-free survival is only 60% in patients receiving either no adjuvant therapy (for those patients deemed to be at high risk because of the presence of grade 3 histology) or intraperitoneal phosphorus 32 (for those patients with one or more other high-risk features present). This 40% relapse rate has caused many to conclude that a no-treatment control arm in any trial involving these patients would be unethical. There is as yet, however, no randomized trial that documents the value of any form of adjuvant therapy.

This situation raises several pertinent questions for the physician: First, should the physician recommend that patients at high risk for recurrence receive adjuvant treatment? In the absence of a definitive trial demonstrating the value of such therapy, the patient...
should always be considered for a clinical trial. If the patient refuses the study or is ineligible, it is then reasonable to consider adjuvant treatment to prevent relapse.

Secondly, what constitutes a rational trial design? Must the trial have a no-treatment control arm? While a no-treatment control arm would be ideal for any study of high-risk patients, such a design is not practical, at least in the United States, because of bias in the medical community that adjuvant therapy must be given. Current and planned protocols in the United States all include treatment in each study arm. Such trials can still yield useful information, particularly if one of the treatment regimens produces a dramatic improvement in survival in a well-characterized high-risk population. Thirdly, what adjuvant treatment should be recommended outside of a clinical trial? Alternatives include: radiotherapy in the form of either intraperitoneal phosphorus 32 or whole-abdomen radiation, or systemic chemotherapy. Whether radiation represents a reasonable alternative is not clear. The trial of the Italian Interregional Cooperative Group of Gynecologic Oncology cited in the review shows platinum-based systemic chemotherapy to be superior to intraperitoneal phosphorus 32, at least in terms of disease-free survival for patients with high-risk features other than grade 3 differentiation. The only randomized trial of whole-abdomen radiotherapy vs platinum-based chemotherapy to be published did show the chemotherapy to be superior, but unfortunately suffered from problems in trial design. In short, the use of adjuvant radiation is not supported by solid scientific evidence.

The use of platinum-based systemic chemotherapy is, however, supported by the data from the previously mentioned Italian study. This trial shows a clear-cut advantage for platinum-based adjuvant therapy vs either no adjuvant therapy or intraperitoneal phosphorus 32, at least in terms of disease-free survival. Whether this will eventually translate into an overall survival advantage remains to be seen. These data do, however, provide a reasonable basis for the physician to recommend platinum-based systemic chemotherapy as adjuvant treatment for patients at high risk for recurrence. If, in fact, such treatment is to be recommended, it is also reasonable to recommend that the best platinum-based regimen (a platinum compound plus paclitaxel [Taxol]) be used.

**Summary**

In summary, a rational approach to the management of early ovarian carcinoma assigns patients to either high-risk or low-risk categories based on findings at a detailed staging laparotomy. The high-risk category is defined as a patient population with one or more of the following high-risk features: grade 3 differentiation, clear cell histology, large-volume ascites, aneuploidy, dense adherence, positive peritoneal cytology, ruptured capsule, tumor excrescences on the surface of the ovary, or extra-ovarian disease. Patients at low risk require surgery only. Those at high risk should receive adjuvant platinum-based chemotherapy (a platinum compound plus paclitaxel). Schilder and colleagues are to be congratulated for a review that summarizes the available information necessary to elucidate such a management scheme.

**Source URL:**

**Links:**