Use of Predictors of Recurrence to Plan Therapy for DCIS of the Breast

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The power of the VNPI lies in the fact that it utilizes a combined assessment of histopathologic variables, tumor size, and tumor margins to provide risk estimates. All of these parameters have been individually implicated in increasing the risk of recurrence for DCIS patients,[1-6] but the VNPI clarifies how to combine them. The strengths of this system are that (1) it allows patients to be classified utilizing routinely gathered information and (2) it employs a very simple scheme to combine these data to produce subgroups with distinct prognoses.

What are the weaknesses of the VNPI? The principal weakness is that it is derived from retrospective data from patients treated, for the most part, at a single center. Thus, the index does not yet adequately control for biases based on differences in pathologic scoring and different definitions of margins. The validation set of 79 patients of Dr. Lagios is not large enough to assess the accuracy of the predictions of outcome for the several subsets of patients.

Accuracy of Risk Estimates

Can the clinician assume that this index will give accurate estimates of recurrence risk at his or her center? Not necessarily. Of particular concern is the reproducibility of the meticulous method used to define the margins in Van Nuys. This method required a more extensive sectioning and examination of margins than are done at many centers. Another issue is that tumor size determinations can be difficult to make. Finally, a bias may also have been introduced by the fact that patients selected among different therapeutic options without randomization. The obvious solution to the question of the accuracy of this index is to assess its accuracy in prospective clinical trials,[7] and there are plans to do this.

A small point that some clinicians would not agree with is the advice to emphasize to the patient that she has a "preinvasive" lesion, unless this is balanced (as the authors recommend) by the fact that there is an ~ 0% mortality at 10 years in mastectomy patients but perhaps as high as a 2% overall mortality in patients who have breast preservation. Patients who elect breast-sparing therapy need to know that recurrences are not always successfully treated, and that about half of these recurrences are potentially lethal.

Clinical Utility of Study Findings

Is the information provided by this study of immediate clinical utility? Yes, but in a limited fashion. The study shows that small, well-differentiated tumors with unambiguously negative margins have an excellent prognosis, and that breast-sparing surgery is quite safe in this population. Conversely, patients with large, poorly differentiated tumors with questionable margins have such high levels of risk (even with radiation therapy) that breast-sparing surgery is problematic. For the very questions for which the index has its greatest potential utility--namely, to help select therapy for patients with intermediate-risk tumors, and to guide decisions about whether radiation can be eliminated from the treatment plan of some patients--the index needs to be validated before it can be accepted uncritically.

One of the special features of this article is that it beautifully illustrates the contributions that can be made by a single center when a well-designed set of therapeutic protocols is followed and follow-up data are carefully collected. To make major contributions, it is not necessary to conduct studies within the structure of the more cumbersome mechanisms of cooperative groups (which may be
ideal for hypothesis validation rather than hypothesis generation). Such contributions can and often are made when local collaborators, utilizing a standardized set of therapeutic options, see enough cases to address a clinically important question in a statistically meaningful way. More opportunities for this type of contribution will arise as large managed-care treatment organizations adopt guidelines. But these opportunities will be realized only if these organizations support forward-thinking individuals within them with funding for long-term patient tracking and, at times, for measurements or procedures that are beyond the present standard of care. Such an investment was made by Dr. Silverstein's team to the benefit of us all.

References:

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