The stages of breast cancer range from 0 to IV. In proper usage, “stage” describes the cancer at diagnosis, although “stage” is also loosely used to describe cancer progression. For example, a stage II cancer is sometimes said to have progressed to become stage IV (but not stage III).

Stage 0 breast cancer (ductal carcinoma in situ) is in a class of its own. Stage IV is also an outlier, being based entirely on the presence or absence of metastatic disease at diagnosis. (The assumption is that, in the presence of metastatic disease, size and axillary nodes are irrelevant.) The three intermediate stages (stages I–III) are based on tumour size and the presence or absence of involved lymph nodes. If patients with ductal carcinoma in situ or with metastatic disease are excluded, staging in its basic form is a simple transformation in which the elements of a 3×2 table are reduced to a single variable with 3 possible values (Table I).

Inspection of this simply constructed table, based on recent American Joint Committee on Cancer categories, reveals that

- the only result of combining nodes (positive or negative) and size (<2 cm or >2 cm) into a single variable is to reduce the number of categories from 4 to 3, and
- the only contribution of size is the creation of a cut-off at 2 cm.

Once this system was recognized as being too simple and not particularly helpful, more subcategories (IA, IB, IIA, IIB, IIC) were created, thus rendering the staging both cumbersome and difficult to remember. The TNM system is a further elaboration, which takes the staging concept well beyond its logical boundaries. T, with its 18 categories, is a measure of tumour size, except when it is Tis or T4, which also indicates invasiveness—for example, in situ or having inflammatory features. The nodal involvement (N) is based either on location and movability, but not number involved (“clinical N”); or on number involved, which is a parameter in a parallel category (“path N”)—but never both. M indicates 3 categories of metastasis. From that system there emerges a highly granular description of a given tumour that borders on personalized medicine. Does pT1cN1Mx reveal more than stage II? Is it really more helpful than simply recording the size and number of nodes?

The original staging system was designed to facilitate comparisons. Changes in stage distributions from year to year and from country to country can be useful indicators of improvements in screening, both in sensitivity and uptake, or of other factors such as increased patient awareness or improved access to care. In screening trials, “downstaging” refers to a promising change in the distributions of stages in screened compared with unscreened women. And in comparing a new treatment with an old treatment, it is important to adjust for possible differences in inherent risk of recurrence and to evaluate benefit in subgroups of patients with different inherent risk. Staging is most useful when it allocates patients into groups of roughly equal size with different prognoses. Based on the understanding current in the 1970s of various cancers, it seemed that most epithelial cancers had a similar natural history, and applying

<table>
<thead>
<tr>
<th>Table I</th>
<th>Breast cancer stage by tumour size and node status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumour (cm)</td>
<td>0 to 2</td>
</tr>
<tr>
<td>Negative Nodes</td>
<td>I</td>
</tr>
<tr>
<td>Positive Nodes</td>
<td>II</td>
</tr>
</tbody>
</table>

*a Adapted from BreastCancer.org, Ardmore, PA, U.S.A.*

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*a This guest editorial is part of a series, titled Countercurrents, by Dr. Steven A. Narod. Series Editor: William D. Foulkes MB BS PhD, McGill University, Montreal, QC.*
a single system to a range of cancer types seemed like a good idea.

In 2012, the weaknesses of formal staging and the complexities of TNM diminish the utility of those systems. To the non-oncologist, is it not better to simply record the tumour size in centimeters and the number of positive nodes? Both variables are important, but they are not interchangeable. The relationship between size, nodes, and prognosis varies for different tumour types. For example, women with small tumours and involved multiple nodes appear to be in a category of intrinsically aggressive cancers. More can be learned about the impact of size on prognosis by dividing cancers into multiple categories rather than into two categories based on a 2-cm cut-off, and much more can be learned by knowing the actual number of involved nodes than by dichotomizing them. The prognosis of a given patient depends continuously with the number of positive nodes, and for patients with cancers of a given size, there is a much smaller difference in prognosis in moving from 0 positive nodes to 1 positive node than from 1 positive node to 10. Prognostic factors that are related to the breast and not the cancer—and that are often overlooked—include the age of the breast and mammographic density.

It is also difficult to accommodate classical staging to new categories. For cancers of equal size and concordant nodal status, the rates and timing of recurrence vary with estrogen receptor status. This year, a collaborative research group from Canada and the United Kingdom reported that they could distinguish 10 separate types of breast cancer, each associated with a different prognosis. Their paper was brought to the public eye and heralded as an important step in fulfilling the promise of personalized medicine. But to follow those early findings with proper clinical studies, clinicians will have to systematically integrate the 10 new categories with traditional prognostic markers. Perhaps a simple trivariate classification scheme will do: size, nodes, and cluster.

Recall that there are two types of prognostic factors: those that indicate the state of advancement of a tumour and those which indicate its relative aggressivity. Tumour size and the number of affected nodes will always be relevant because they belong to the first category—they underpin the concept of “early” diagnosis. The molecular markers such as the 10 new clusters or the results of PAM50, MammaPrint (Agendia, Irvine, CA, U.S.A.), or Oncotype DX (Genomic Health, London, U.K.) are used to subclassify tumours by their intrinsic metastatic potential and are, by and large, stable throughout the natural history of the cancer. I do not anticipate that the addition of new molecular markers, singly or in combination, will render size and nodes redundant. On the other hand, if size, number of positive nodes, and the intrinsic malignant potential of the cancer are known, what additional information is gained from tumour stage? Beyond size and nodes, important additional information comes from indices of proliferation and invasiveness. I think that clinician–scientists will benefit if pathologists and clinicians adapt to the changing landscape by routinely incorporating size in centimetres and the number of positive nodes into clinic notes.

REFERENCES


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