The reliability of sampling three to six nodes for staging breast cancer

Gábor Cserni

Abstract
Aims—To test the hypothesis that a correct qualitative assessment of axillary nodal status can be established by examining only a limited number of lymph nodes.

Methods—Slides from 499 pN1 or pN0 axillary dissection specimens relating to symptomatic breast cancer cases operated on at our institution between 1991 and 1996 were reviewed. Nodes were ranked in descending order on the basis of their estimated size and lymphoid or metastatic tissue content. After ranking, all nodes were studied microscopically; 265 axillary clearance specimens were positive.

Results—Assessment of the 3–6 largest/firmest nodes can lead to the detection of 93–98% of node positive patients and can give a correct qualitative assessment of axillary node status in 90–99%.

Conclusions—Sampling the 4–6 largest/firmest nodes seems to be a reliable alternative for the staging of symptomatic breast cancer. These results suggest a reconsideration of the generally held view that a minimum of 10 nodes is required for adequate identification of the pN0 category.

Keywords: axillary clearance; axillary sampling; breast cancer
Table 1 Rates of detection of positive nodes when only the first three, four, five, or six largest/firmest nodes were examined and the accuracy of this approach, expressed as the percentages of cases adequately identified, in comparison with the results of an assessment of the total number of nodes in the clearance specimen

<table>
<thead>
<tr>
<th>Number of lymph nodes assessed</th>
<th>3 Nodes</th>
<th>4 Nodes</th>
<th>5 Nodes</th>
<th>6 Nodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive axillary nodes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive nodes only; n=265</td>
<td>236 to 246</td>
<td>250 to 257</td>
<td>253 to 259</td>
<td>258 to 261</td>
</tr>
<tr>
<td>Per cent of group A</td>
<td>89–93%</td>
<td>94–97%</td>
<td>95–98%</td>
<td>97–98%</td>
</tr>
<tr>
<td>Positive nodes only; n=499</td>
<td>94–96%</td>
<td>97–98%</td>
<td>98–99%</td>
<td>99%</td>
</tr>
</tbody>
</table>

265 axillary clearance specimens were positive (set A) from the 499 involved in the study (set B). Rates of concordance with the qualitative axillary nodal status established from the samples of the three to six largest nodes were expressed as percentages of the node positive cases (A) and of all the specimens (B) in table 1. As identical serial numbers were assigned to nodes of the same estimated size, the number of cases matching the qualitative axillary nodal status (positive or negative) was given as a range (for example, metastasis in only one of the two nodes 3–4 could either be identified by assessing three nodes or be missed).

The mean number of lymph nodes per axillary specimen in this study was 10.7 (range 1–45), while the mean number of metastatic nodes was 2.5 (range 0–43).

Discussion

With this system of serial numbering the lymph nodes on the basis of their estimated size and firmness, it was possible to show that the histopathological assessment of only four to six nodes furnishes a reasonably acceptable alternative evaluation of qualitative axillary node status. This appears to compare favourably with mathematical models (considering all randomly selected nodes as equivalent), which state that at least 10 to 11 nodes should be examined for a reliably negative (accuracy 90% or above) qualitative axillary nodal status. This latter requirement does not take into account qualitative features of the lymph nodes such as size, consistency, or localisation, and this has resulted in a predominantly mathematical approach to what is a complex biological problem. Localisation is also neglected in this model which examines the 3–6 most obvious nodes, but the other features are not neglected. Such a sampling approach could result in a reduction in the minimum number of lymph nodes required for reliable staging as node negative disease without diminishing sensitivity.

The results reported here raise several issues. First, they provide further evidence of the reliability of taking out the four to six most obvious nodes during axillary surgery for breast cancer. Although this study did not test the ability of the surgeons to identify the most obvious nodes, it is presumed that the nodes identified as the largest ones in this study are identified with high confidence by surgeons during the operations. Most surgeons who sample the axilla take nodes from level I, but a failure to find the required number of nodes at this level would usually result in a search for palpable nodes at level II, and this is why the failure to separate the analysed nodes into levels should be only a minor limitation in this study.

Second, it is also likely that the nodes estimated as being the most obvious ones in this study are also those that a pathologist would identify as such when cutting up an axillary clearance specimen. This is why node negative cancers diagnosed as such from six to seven nodes should not be considered inadequately staged because of the seemingly suboptimal number of lymph nodes assessed, since the most obvious nodes were probably examined. This conclusion also highlights the erroneous oncology practice of giving regional radiation treatment to the axilla when node negativity was established from less than 10 nodes from an axillary clearance specimen.

Third, the method of sampling the four to six most obvious nodes in the histopathology laboratory could be an alternative cost sparing approach for the evaluation of axillary clearance specimens in poorer countries. This alternative should be further tested, since most authorities would be against such a “negligent” pathology work up, and most recommend the recovery of as many nodes as possible from the axillary fat. In a previous study based on an earlier period than the one reported here, we found that more than half of our specimens had a seemingly suboptimal number of lymph nodes recovered and examined microscopically (an average of seven nodes per axillary specimen). By applying a mathematical model, we concluded that at least 10 nodes must be examined for a reliable identification of the pN0 category. We then audited the process of cutting up and raised the average number of lymph nodes per specimen to 22. By applying the same mathematical model to these cases, the suggested minimum number of lymph nodes to be investigated increased to 27, with all specimens having 10–42 nodes examined. However, the assessment of more nodes did not seem to influence the rate of detection of node positive tumours, and indicated that fewer than 10 nodes could also give a reliable histopathological staging of breast cancer.

Clinical evidence of the truth of our first assumption comes from several studies. Lymph node sampling is a diagnostic procedure used in several countries, for example the United Kingdom and Denmark. It is a term applied to different methods of removing axillary lymph nodes for staging (prognostic) purposes. Because of the multiplicity of techniques and the meaning of “axillary sampling,” published reports have been contradictory, some studies suggesting reliability and others a high error rate. Such a high error rate may in fact result from poorly performed surgery. It appears that sampling and histological work up of the four to six largest/firmest lymph nodes identified by the surgeon during the operation is a reliable alternative method of staging breast cancer.

In view of the data supporting the value of axillary sentinel lymph node biopsy for staging, it is important to note that the
Fewer lymph nodes for staging breast cancer

nodes draining the tumour usually enlarge as a consequence of reactive hyperplasia caused by preoperative diagnostic interventions (aspiration or core biopsies), and this makes them easier to palpate during sampling. This may cause an overlap with sentinel lymphadenectomy in cases without properly performed lymphatic mapping. Our preliminary data on 40 consecutive breast cancer patients undergoing sentinel lymphadenectomy before completing dissection suggest that the sentinel lymph node identified by patent blue mapping is in most cases (>95%) included among the six largest/firmest nodes, defined by the same way as in this study. We are aware of another study using gamma probe guidance for identifying the sentinel lymph nodes in which investigators found a 72% overlap between the sentinel nodes and a four node sample performed before using the gamma probe. 26

In the present era, when lymphatic mapping and sentinel lymphadenectomy is apparently the best approach to staging early breast cancer, such a sampling procedure could be followed in cases where no sentinel lymph node has been identified or where there are multiple tumours, when identification of sentinel lymph nodes may be unreliable. 27 This reduction in the number of nodes assessed could also make the more sensitive methods of detecting axillary metastases (serial sectioning, immuno-staining) more cost-effective. Patients with positive axillary sampling could then be treated by either irradiation 28 or therapeutic dissection. In this way, patients with node-negative tumours could avoid axillary dissection and its possible morbidity without loss of axillary node status, which remains the most powerful predictor of prognosis.

A possible drawback of these results is that they were obtained on breast cancer cases with palpable tumours. However, the results produced by sampling in the United Kingdom indicate that this method may also be of value in cases detected by screening.

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