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The Impact of Axillary Lymphadenopathy on Further Treatment in Breast Cancer? A Model for Clinical Staging

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Clinical assessment is an important part of the breast cancer patients' work-up, but it has low sensitivity and specificity. In a retrospective study, histological slides of axillary clearance specimens were used to model palpability of the axillary lymph nodes. Obvious nodes (enlarged and involving considerable amount of lymphatic and/or metastatic tissue) and nodes equal to or larger than 1 cm or 1.5 cm were counted and the slides were subsequently reviewed. The false positive and negative rates expected on the basis of the model ranged from 24 to 72% and from 10 to 38%, respectively. This model (also valid for intraoperative assessment of nodal status by palpation) documents the lack of specificity of clinical staging of the axilla. These results question the practice of excluding patients with palpable axillary lymph node enlargement from less radical staging procedures such as axillary sampling or sentinel node biopsy (Pathology Oncology Research Vol 4, No 4, 301–303, 1998)

Key words: breast cancer, axillary metastasis, clinical staging, sampling, sentinel lymph node biopsy

Introduction

Clinical examination of the axilla is an important part of the initial physical assessment of breast cancer patients. Despite the low sensitivity and specificity of this method of staging[6,7] it continues to influence further treatment planning. Those patients that present with axillary lymphadenopathy on palpation are often excluded from less radical management protocols, and axillary clearance is advocated to them, even by people favoring axillary sampling or sentinel lymph node biopsy for staging purposes.[1,9] The rationale for these latter procedures is far beyond the scope of this paper and readers are referred to reviews of the subject.[3,8,9,10]

We have carried out a retrospective study for modeling clinical assessment of the axilla to see whether the nodal status gained by physical examination can unquestionably be exclusive for lesser surgical staging interventions or not.

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Materials and methods

Histopathology reports of the archives of Bács-Kiskun County Teaching Hospital, Department of Pathology were reviewed and breast cancer cases treated by mastectomy or breast conserving surgery and axillary dissection between 1991 and 1996 were retrieved. Cases with pN0 and pN1 categories of the UICC TNM system[11] were selected, and all slides of the axillary lymph nodes were reviewed.

Originally lymph nodes were recovered from the axillary fat without clearing and processed separately. The largest cut surface was always sectioned and studied under the microscope after haematoxylin and eosin (HE) staining.

Obvious nodes were identified on the basis of their largest cut surface. A node was considered obvious because of its size and/or firmness suggested by its lymphoid or metastatic neoplastic tissue content. Only lymph nodes above 9 mm in largest dimension could be classified as obvious. Categorizing a node as obvious had a subjective component despite the above criteria, but it was assumed that this category reflected the best the palpability of the lymph nodes preoperatively, during surgery and in the cut-up room of the histopathology laboratory.

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Table 1. **Distribution of obvious nodes in relation to axillary nodal status**

Nodal status	*All axillas*	*Axillas with obvious nodes* positive *for metastasis*	negative
Negative	234	0	120
Positive	265	196	96
All	499	196	216

As a more objective criterion for categorizing, lymph nodes equal to or larger than 1 cm and 1,5 cm in their largest dimension were also counted and recorded.

After sorting the nodes in the above categories, all slides were reviewed, and the number of nodes positive or negative for metastases were recorded separately in each case and category.

Results

The relationship between obvious nodes and qualitative histopathologic lymph node status (positive or negative for metastasis) is shown in *Table 1*.

218 of patients with metastatic nodes (82.3%) could have been clinically identified with palpation of either positive or negative obvious nodes. 120 patients (24%) would have been falsely classified as positive for disease metastatic to the axilla on the basis of the presence of obvious negative nodes and 47 patients (9.4%) would have been falsely classified as negative on the basis of the absence of obvious nodes.

The number of lymph nodes 1 cm or larger and 1.5 cm or larger in their greatest dimension and their relationship with the qualitative axillary nodal status are presented in *Table 2* and *3*, respectively.

239 patients representing 90.2% of positive axillas could have been identified by palpation of positive (198) or negative (41) lymph nodes with largest dimension of 1 cm or larger. The rate of missing patients with disease metastatic to the axilla by this technique and the false positive rate would have been 26/265 (9.8%) and 169/234 (72.2%), respectively.

142 patients representing 53.6% of positive axillas could have been identified by palpation of positive (118) or negative (24) lymph nodes with largest dimension of 1.5 cm or larger. The rate of missing patients with disease metastatic to the axilla by this technique and the false positive rate would have been 123/265 (46.4%) and 79/234 (33.8%), respectively.

The relationship between axillary nodal status determined by histological assessment of the clearance specimen and the presence of negative lymph nodes belonging to either category in the absence of positive nodes in the same category is displayed in *Table 4*. This gives a good idea of the false positive rates on the basis of our model.

Discussion

The presence of obvious nodes (as a subjective approach) or the presence of lymph nodes equal to or larger than 1 cm or 1.5 cm (as more objective approaches) give rather high false positive or negative rates. Increasing the threshold for defining a lymph node as enlarged from 1 cm to 1.5 cm increased the specificity but reduced the sensitivity of the model.

Our model, taking into account the expected lymph node consistency and size (for obvious nodes) or size alone, seems valid not only for the preoperative assessment of nodal status by palpation, but also for intraoperative assessment by the same way and macroscopic assessment of the nodes at the histopathology lab.

Table 2. **Distribution of lymph nodes >= 1 cm in relation to axillary nodal status**

Nodal status	*Number of positive nodes >= 1 cm*							*negative nodes >=1 cm*						
	0	1	2	3	4	5	>5	0	1	2	3	4	5	>5
Negative	234	0	0	0	0	0	0	65	74	46	29	7	7	6
Positive	67	90	41	25	16	11	15	121	90	37	11	4	1	1

Table 3. **Distribution of lymph nodes >= 1.5 cm in relation to axillary nodal status**

Nodal status	*Number of positive nodes >= 1.5 cm*							*negative nodes >=1.5 cm*					
	0	1	2	3	4	5	>5	0	1	2	3	4	5
Negative	234	0	0	0	0	0	0	155	56	19	4	0	0
Positive	147	69	30	10	5	2	2	219	40	4	1	0	1

Table 4. **Presence (yes) or absence (no) of negative lymph nodes in a given category in the absence of positive lymph nodes in the same category**

Nodal status	*Categories*					
	Obvious nodes		*Nodes >= 1 cm*		*Nodes >= 1.5 cm*	
	yes	no	yes	no	yes	no
Negative	120	114	164	70	79	155
Positive	22	243	41	224	24	241
All	142	357	205	294	103	396

From this study, just as from previous studies comparing preoperative clinical nodal status to the gold standard of histopathology, it emerges that clinical staging has unacceptably high false negative and positive rates.[4,6,7,12] Having axillary lymphadenopathy does not mean having axillary metastasis, and the lack of obvious nodes on palpation does not mean the absence of such nodes. The value of axillary palpation in obese patients is even smaller.

While physical examination is a mandatory part of the patients' work-up, because of its low specificity (and sensitivity) it should not influence further treatment of early breast cancer patients by itself. Our current practice of lymphatic mapping and sentinel lymph node biopsy[5] also gives support to this concept. We perform mapping even in cases of palpable axillary lymphadenopathy, and sometimes the cleared axilla turns out to be negative after detailed examination of the sentinel node and routine examination of the non-sentinel nodes.

There are certainly some exceptions to the above suggested rule, such as the presence of an obviously metastatic conglomerate in the axilla; but this is most often seen in larger tumors where axillary clearance is often indicated *ab ovo*, as the lack of metastasis is exceptional in these cases.[13]

The role of clinical staging increases in trials where no other methods of evaluating axillary spread are used, but this may not influence the treatment even in such cases.[2]

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