Is breast cancer axillary dissection still needed?

Carlos Freire de Oliveira and Margarida F. Dias

Breast cancer patient's prognosis depends on: a) adequate diagnosis procedures allowing the detection of non-palpable small lesions; b) proficient surgical techniques performed by an expert surgeon belonging to a multidisciplinary team; and c) access to updated strategies of adjuvant treatments. Axillary surgery on breast cancer first stages still is a subject of controversy, mainly concerning tumours <2 cm, and especially <1 cm.

In spite of the former controversy concerning axillary dissection, last St. Gallen Conference (2001) has considered the axillary involvement, as well as the number of positive nodes, as the two most relevant factors in breast cancer treatment. British Association of Surgical Oncology (1998) guidelines established that histological node status must be obtained in at least 90% of planned curative operation. European Society of Surgical Oncology guidelines reported that a minimum of 4 nodes, and preferably 10 nodes should be excised for examination in axillary dissections.

As suitable arguments to perform axillary dissection should be considered that it is an important staging procedure in patients with early breast cancer and the most important prognostic factor in breast cancer recurrences and survival. Axillary dissection permits a qualitative as well as a quantitative evaluation and determines the decision concerning adjuvant chemotherapy and, based on the number of involved nodes, regulates the chemotherapy dose intensification.

On the contrary, potential disadvantages of axillary dissection include the debatable therapeutic value since alternative treatment exist such as axillary irradiation. Furthermore, in T1 breast cancer patients more than 75% are node negative and in older patients with small ER positive tumours nodal status does not affect therapeutic strategies. Axillary dissection is also responsible for major post-surgical sequela in breast cancer surgical treatment, increases the overall cost of treatment and, after all, it can be replaced, in terms of prognostic information, by alternative less invasive procedures.

In T1 breast cancer node involvement is related to tumour size. Lagares-García refers the mean tumour size of 1.48 cm considering T1 node positive tumours and 1.25 cm considering T1 node negative tumours. García observed that 76% of node positive tumours were classified as T1c; on the other hand, only 54% of node negative tumours were T1c and the remaining tumours T1a and T1b. Besides, this author has registered axillary node invasion in 7% of T1a tumours, in 13% of T1b and 25% of T1c, referring a slightly shorter 5 years overall survival of axillary metastatic tumours.

Recent studies considering tumours <1 cm concluded that 18% to 22% of breast tumours were classified as T1a and 78% to 82% as T1b. The rate of axillary invasion varies from 11% to 22% and ER has been considered positive in 80% to 85%1,4. In the Lagares-García analysis1 no significant difference was observed concerning 5 years survival when comparing T1a and T1b tumours, but a slightly shorter 5 years overall survival for T1c tumours.

In table 1 are represented several studies concerning breast tumours <1 cm and the corresponding overall survival of follow-up periods of 7 to 20 years was 85% to 100%.

An important feature is the false axillary status that varies in different published studies in ranges of 0.5% to 29%, depending on the mean number of excised axillary nodes.

A node-negative patient with primary breast cancer should be defined as a patient with ≥10 lymph node removed and negative from the axilla at the operation. According to Veronesi et al4, in a population of 851 T1 breast cancer patients, 49% were considered node positive, 17% presented 1 invaded node, 14% presented 2 or 3 invaded nodes, 11% presented 4 to 10 invaded nodes and 7% presented more than 10 metastatic nodes.

Besides tumour size, axillary node invasion in small tumours is considered to be associated to other factors. In a univariate analysis, Rivadeneira et al2 considered patient's age (<50'), tumour size, lymphatic invasion
Veronesi\textsuperscript{7} has found the average number of lymph nodes from a complete axillary dissection is 20.3: 13.5 from level I, 4.5 from level II and 2.3 from level III. Recently, Saha\textsuperscript{8} confirmed this data referring an average number of 10 lymph nodes from level I, 6 from level II and 4 from level III. According to this Italian data, in patients with axillary metastases, 54.2% arises from level I, 22.5% from levels I+II, 22.2% from levels I+II+III and 1.2% from level II and 0.1% from level III. They concluded this way that metastatic involvement of levels II and III is absolutely exceptional when level I is free of metastases. The probability of invasion of the II level when a single node is involved at the I level is 12.1%; this probability increases to 19.5% if 2 nodes are involved, 57.5% if 3 nodes are involved and 40.3% if 4 nodes are involved at level I.

Table 2 presents 6 published data from different years. It is very clear that the extent of axillary surgery and the number of removed nodes varies significantly. The mean number of surgically excised lymph nodes is not related to the surgical technique like Haustad, Patey, quadrantectomy and axillary dissection together or separately; it is mainly related to the surgeon's experience and to the multidisciplinary approach, as the statement of Danish Breast Cancer Cooperative Group\textsuperscript{10}. In Odense, axillary dissection was performed by multidisciplinary teams and surgical guidelines and in other danish institutions it was performed by individual surgeon; in Odense 50% of the axillary dissections revealed >10 lymph nodes but in the rest of DK 10 or more nodes were obtained in 18% of the axillary surgery and this difference was statistically significant. In 10 years follow-up a significant difference was observed on what concerns overall survival, favorable to Odense.

A randomized study of U, Chetty et al\textsuperscript{11} (fig. 1) concluded that in axillary node involvement high-risk patients it should be performed an «axillary clearance» with an average of 15 excised nodes; in intermediate risk patients a similar «axillary clearance» or an axilla sample and radiation (average 5 nodes) should be performed; in low risk patients the axilla «sample» should be enough. Morbidity following axillary lymph node dissection includes: seroma formation, arm lymphedema (5%-50%), arm numbness (60%-70%), arm weakness (20%-25%), pain (25%-50%) and arm stiffness (5%).

Valid alternatives to axillary lymph node surgical dissection should be considered based on the evaluation of the prognosis according to the primary breast carcinoma characteristics, performing post-operative regional irradiation and to the lymphatic mapping and sentinel node biopsy.

### Table 2. Axillary dissection extension. Average number of excised lymph nodes

<table>
<thead>
<tr>
<th>Author</th>
<th>No. pts</th>
<th>Years (Stage)</th>
<th>Nodes (Average, Range)</th>
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</thead>
<tbody>
<tr>
<td>Graverson</td>
<td>3,128</td>
<td>77-82</td>
<td>I-II (4, 0-30)</td>
</tr>
<tr>
<td>Grabau</td>
<td>586 (OD)</td>
<td>80-90</td>
<td>I (10, 1-31)</td>
</tr>
<tr>
<td></td>
<td>11,953 (DK)</td>
<td>80-90</td>
<td>I-II (6, 0-40)</td>
</tr>
<tr>
<td>Veronesi</td>
<td>1,446</td>
<td>83-86</td>
<td>I-II (20.7, 0-40)</td>
</tr>
<tr>
<td>Wong</td>
<td>722</td>
<td>68-67</td>
<td>I (11, 6-67)</td>
</tr>
<tr>
<td>Saha</td>
<td>362</td>
<td>84-93</td>
<td>I-II (21, 4-58)</td>
</tr>
<tr>
<td>Hetelekdis</td>
<td>1,406</td>
<td>68-86</td>
<td>I-II (10, 1-39)</td>
</tr>
</tbody>
</table>

Rev Oncol 2002; 4 Suppl 2:33-53
Menard et al. evaluated prognostic factors on 465 primary breast carcinomas from patients without palpable lymph nodes: tumor size, grading, c-erbB-2 over expression and laminin receptor expression. A score was performed (1 to 4) and a good correlation was found when comparing score value, lymph node involvement and overall survival. Recently, these authors conducted a prospective non-randomized study concerning T1 and T2N0 breast cancer patients who underwent breast surgery without axillary dissection. The prognostic value of the referred score as a predictive factor of axillary node relapse or distant metastases was confirmed (table 3).

Concerning post-operative regional irradiation, the NSABP trial concluded that there is a decrease in the incidence of distant metastases in patients with clinically negative nodes submitted to total mastectomy and axillary radiation when compared to patients submitted to total mastectomy or radical mastectomy, in a 10-years follow-up. Patients with clinically positive nodes showed no difference in terms of local or distant metastases according to the therapy in a 10-years follow-up.

Giuliano et al. and Krag et al. have developed a new technique to identify the sentinel node, as the first draining lymph node. Different techniques still are subject of controversy and open questions persist like the radiopharmaceutical to be used, the dose of radiactivity, the ideal probe, the site of injection, the blue dye, learning curve, the pathological assessment of the sentinel node and the results of randomized trials. Veronesi et al. evaluated 373 patients outside research protocols: sentinel node was identified in 99% and it was considered positive in 24.9%; this study registered 2.4% of false negative results on frozen sections and 43.6% of micrometastases in positive nodes.

Data presented allows us to conclude that main indications to perform axillary lymph node dissection in initial breast cancer are: a slight survival advantage (about 5 to 9%), an accurate staging, an effective regional disease control and a prognostic information. Axillary dissection should always be performed when we notice clinically palpable lymph nodes and in recurrent palpable axillary nodes, if the axilla has not been previously dissected.

Indications for avoidance of axillary dissection are: no impact on survivals out come, decreased morbidity, decreased expenses and no need for axillary dissection if selection for adjuvant therapy can be performed on the basis of the primary tumors.

Given the results, T1a and T1b invasive breast carcinoma may still require axillary dissection. We wait for the conclusions of randomized studies to determine the real value of the sentinel node biopsy on these cancers.

References
Diagnostic value of ultrasound and color doppler in identifying axillary lymph node metastases in patients with breast cancer-preliminary results

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Purpose. The aim of this study is to evaluate the diagnostic ability of ultrasound and color Doppler in axillary lymph node metastases of patients with breast cancer.

Methods. Prospective study including 52 patients with primitive, invasive, node negative breast cancer who underwent preoperative axillary ultrasound and color Doppler. Doppler and morphologic ultrasound criteria were applied to the axillary lymph node metastases identification.

Results. The imagiologic study of all 52 patients identified a total of 84 nodes; 28 were considered to be positive according to the established criteria. The histological examination of the axillary dissection revealed a total of 577 nodes; 27 out of 577 presented metastases. All invaded nodes belonged to 10 patients; the previous imagiologic study was positive for axillary lymph node metastases in 9 out of these 10 patients. A sensitivity of 90.0%, a specificity of 60.8%, a negative predictive value of 93.3% and a positive predictive value of 50.0% were achieved.

Conclusion. The imagiologic study of the axillary region through ultrasound and color Doppler might be useful to assess axillary lymph node metastases in patients with breast cancer.

INTRODUCTION

Surgery has always been the classical treatment of breast cancer. However, the surgical procedure has been, for long, a controversial issue due not only to medical and surgical but also cultural and emotional aspects. Therapeutic strategies for breast cancer have evolved over time and today the surgical approach tends to be more conservative, less aggressive and with lower morbidity.

Recently, the sentinel node technique was introduced1-3 an apparently accurate method for axillary staging in breast cancer, using blue dye and/or radiolabelled colloids. The objective of this technique is to avoid the axillary dissection in selected patients with invasive breast cancer, reserving this procedure only for those with histological positive sentinel nodes or in whom the sentinel node cannot be identified. Nevertheless, this is an expensive, time consuming and invasive technique.

The aim of our study is to evaluate the diagnostic ability of ultrasound and color Doppler, a non-invasive technique, in identifying axillary lymph node metastases in patients with breast cancer.

METHODS

Prospective study carried out at the University Hospital of Coimbra included so far 52 patients. All patients underwent an ultrasound-guided or an open wire-directed surgical biopsy of a breast lesion corresponding to invasive carcinoma. Tumors were T1 or T2, N0 with no indication for neoadjuvant treatment. One of the patients had a bilateral invasive breast cancer.

Fig. 1. Suspicious lymph node showing globular shape, cortical irregular thickening and loss of germinal centre echogenicity.