Is breast cancer axillary dissection still needed?

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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 bellowing 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, specially <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 sequelae 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[1] 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 83%[1-3]. In the Lagares-García analysis[1] 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 83% to 100%.

An important feature is the false axillary status that varies in different published studies in ranges of 0.5% to 20%, 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 al[4] in a population of 831 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 al[2] considered patient's age (<50>), tumour size, lymphatic invasion

TABLE 1. **Overall survival and disease-free survival in breast cancer patients with tumours < 10 mm and receiving no adjuvant treatment**

Authors	Years accrued	No.pts	Follow-up (years)	Outcome %
Rosen, 1981	64-70	171	20	86
Tinnemans, 1989	71-86	18 T1a	10	91
		29 T1b	10	100
Rosner, 1991	76-86	42 T1a	7	92
		49 T1b	7	90 (DFS)
Crowe, 1992	74-85	89	10	80 (DFS)
Stierer, 1992	69-89	138	15	84
Arnesson, 1994	76-89	254	7	99 (DFS)
Leitner, 1995	77-90	218	6.9	93
Quiet, 1995	27-84	113	20	79 (DFS)
Lee, 1997	75-90	88	7.8	92
Moon, 1987	64-80	154	10	83
Fisher, 2001	76-93	1,259	8	85
				73 (DFS)

and tumour grade. Lagares-García[1] considers patient's age, tumour size and ER status. Finally, Wong et al[5] refers as associated factors tumour size, lymphatic invasion and tumour location (lateral vs central). In a multivariate analysis only patient's age and tumour diameter are considered factors associated with axillary lymph node metastases[2].

Greco et al[6] report no significant differences concerning axillary relapse between T1a and T1b tumours: 2% in T1a and 1.7% in T1b. T1c tumours present a statistically significant difference since axillary relapse occurred in 10.5%. Same conclusion is valid on what concerns distant metastases: 5.9 % in T1a, 2.7% in T1b and 15.4% in T1c.

Axillary relapse have been correlated in a higher frequency to G3 tumours with necrosis and higher labelling index. Distant metastases occur mainly in G3 tumours with a high mitotic index, necrosis and higher proliferating index.

Considering this subject, axillary dissection, it is very important to consider the exact number of surgically excised nodes. In 1988, a danish study[7] demonstrated in a clear way a significant decrease of the overall survival concerning patients with 5 nodes removed from partial axillary dissection when compared to patients wich axillary dissection was ≥5 nodes. This observation is related to a higher percentage of «false-negative» axillas and the subsequent absence of adjuvant therapy. These danish authors[3] more recently have demonstrated that when comparing tumours <10 mm and >10 removed nodes with ≥10 removed nodes, the overall survival and the disease-free survival were significantly higher in patients with higher number of removed nodes. However, the previous study NSABP[8] that compared radical mastectomy to total mastectomy and radiation and to total mastectomy alone concluded that in node-negative patients there was no statistically significant difference concerning distant metastases in a 10 years follow-up. The same was not true on wath concerns regional recurrences since they were significantly decreased in patients treated by total mastectomy and radiation. This study also demonstrated no difference related to local and distant relapse in patients with clinically positive axilla submitted to radical mastectomy or to total mastectomy and radiation.

Veronesi[4] 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[9] 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% arised from level I, 22.3% 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 1 single node is involved at the I level is 12.1%; this probability increases to 19.5% if 2 nodes are involved, 37.5% 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 Halstead, 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[10]. In Odense, axillary dissection was performed by multidisciplinary teams and surgical guidelines and in other danish institutions it was performed by individual surgeons; in Odense 56% 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 stastistically 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[11] (fig. 1) concluded that in axillary node involvement high-risk patients it should beperformed 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.

Morbility following axillary lymph node dissection includes: seroma formation, arm lymphedema (5%-50%), arm numbness (60%-70%), arm weakness (20%-25%), pain (25%-30%) and arm stiffness (6%).

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 senstinel node biopsy.

TABLE 2. **Axillary dissection extension. Average number of excised lymph nodes**

Author	No. pts	Years	Stages	Nodes	
				Average	Range
Graverson, 1988	3,128	77-82	I-II	4	0-30
Grabau, 1988	586 (OD)	80-90	I-II	10	1-31
	11,953 (DK)	80-90	I-II	6	0-40
Veronesi, 1990	1,446	83-86	I-II-III	20.7	
Wong, 2000	722	68-87	I-II	11	6-67
Saha, 2000	362	84-93	I-II-III	21	4-58
Hetelekidis, 2000	1,406	68-86	I-II	10	1-39

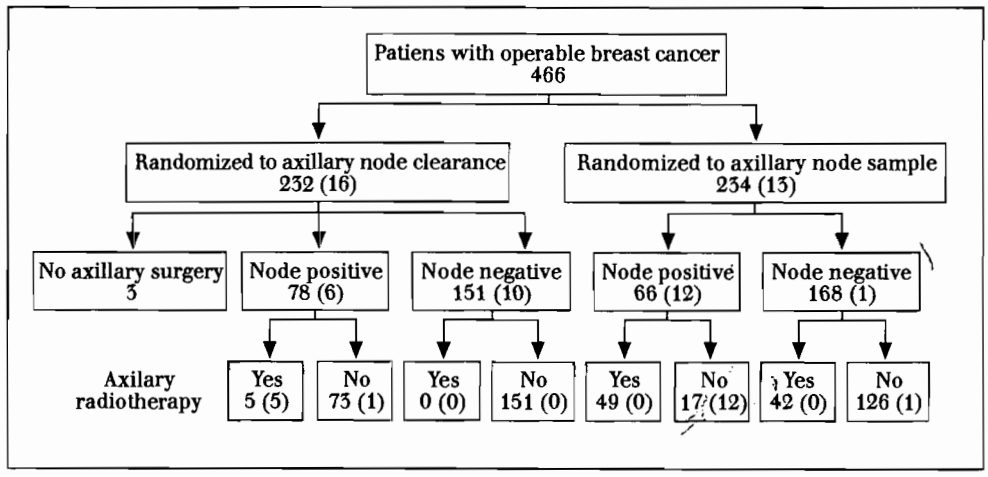

Fig. 1. Management of the axilla in operable breast cancer treated by breast conservation: a randomized clinical trial-Edinburg Breast Unit. Adapted from Chetty U, et al[11].

Menard et al[12] evaluated prognostic factors on 463 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[6] 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 relapses or distant metastases was confirmed (table 3).

Concerning post-operative regional irradiation, the NSABP trial[8] 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[13] and Krag et al[14] have developped a new technique to identtify 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 of radiactivity, the ideal probe, the site of injection, the blue dye, learning curve, the pathological assessement of the sentinel node and the results of randomized trials. Veronesi et al[15] evaluated 373 patients outside research protocols; sentinel node was identified in 99% and it was considered positive in 24.8%; 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 3 to 5%), 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 survgical 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.

TABLE 3. **Alternatives to axillary lymph node dissection. Prognostic value of primary breast cancer characteristics**

Score	Nodal status	No. of cases	Survival (%) after		
			5 years	10 years	15 years
1	NEG	65	95	89	85
	POS	36	94	85	76
2	NEG	83	84	77	64
	POS	74	78	62	51
3	NEG	72	70	58	54
	POS	64	67	49	41
4	NEG	31	76	54	45
	POS	38	49	41	32

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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 32 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 32 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 introduced[1-3], 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 32 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.

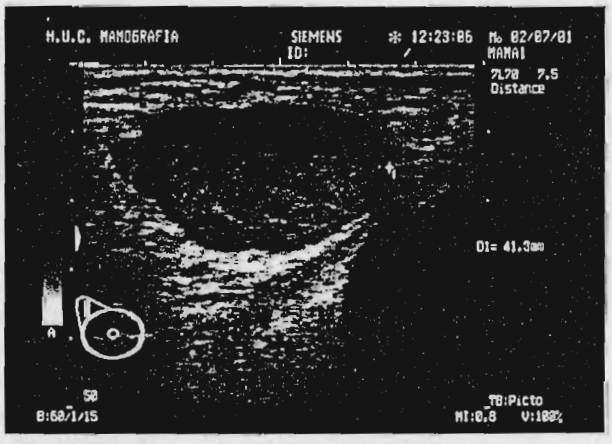

Fig. 1. Suspicious lymph node showing globular shape, cortical irregular thickening and loss of germinal centre echogenicity.