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Sentinel lymph node biopsy and non-sentinel node involvement in special type breast carcinomas with a good prognosis

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ABSTRACT

This study aimed at identifying factors related to sentinel lymph node (SLN) involvement in patients with tubular, cribriform, mucinous or papillary breast carcinoma and those related to non-SLN metastases if an SLN was positive. Multivariate analyses involved logistic and stepwise regressions. The SLNs harboured metastases in 85 of 572 cases, 78 of whom underwent axillary dissection; 19 presented non-SLN positive disease. Lack of lymphovascular invasion, a tumour size ⩽10 mm and a single SLN removed were the factors predicting an SLN metastasis rate <10%, and patients with these features could be candidates for no surgical axillary staging. A positive SLN proportion of ⩽50% and no lymphovascular invasion were associated with a <10% rate of non-SLN invasion; patients with a positive SLN and these features could be candidates for the omission of completion axillary dissection. The opposite presentation of these factors would mandate SLN biopsy and axillary dissection, respectively.

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1. Introduction

Axillary lymph node dissection (ALND) has long been considered the standard surgical procedure with which to stage and treat the axilla of breast cancer patients. As a therapeutic effect cannot even be hypothesised in the absence of a disease, patients without axillary nodal involvement certainly do not benefit from this intervention, but are exposed to its morbidity. Sentinel lymph node (SLN) biopsy (SLNB) has largely replaced ALND in the staging of patients with no clinical, imaging or pathological evidence of regional nodal involvement. Although not perfect in terms of accuracy, SLNB has allowed a selective approach to ALND. Patients with no metastasis in the SLNs can safely avoid ALND,[1] whereas ALND still remains the standard procedure for SLN-positive patients.[2]

Since a relatively high proportion of patients with positive SLNs are found to have no involvement in the remaining axillary lymph nodes, several studies have assessed whether patients with no further axillary disease could be predicted on the basis of the primary tumour and SLN findings. It is tempting to suppose that these patients could be spared an ALND even if the SLN is metastatic. Some patients may have such a low risk of axillary nodal involvement that any type of surgical axillary staging in them may seem unnecessary.[3,4]

Currently, the axillary staging of low-risk patients remains controversial, with several possible options, including observation only, SLNB, axillary sampling and ALND in centres where SLNB or sampling cannot be performed for technical or other reasons.

Certain histological types of breast carcinomas are associated with a good prognosis.[5,6] This study was initiated in order to analyse the SLNB implications in these tumours.

2. Materials and methods

The European Working Group for Breast Screening Pathology has initiated a number of studies related to SLNs.[7–11] Members were recently asked to contribute pathology-related data on their SLNB cases involving special types of breast cancers accepted as having a good prognosis: tubular/cribriform, mucinous and papillary carcinomas. Mixed tumours were not included in the analysis, and a pure histological type required that at least 90% of the tumour had the necessary pathognomonic features. Invasive cribriform and tubular carcinomas were lumped together because some tumours presenting a mixture of these two patterns are called tubular or cribriform, depending on the predominant pattern.[12,13]

The methods of SLNB applied in the different institutions were not uniform, and involved both intraparenchymal (peritumoural and/or intratumoural) and superficial (intradermal or subareolar) injection of the tracers. Patent blue dye and ^{99m}Tc-labelled radiocolloids were used, either in combination or alone. ALND was performed routinely, as part of the SLNB validation phase (in 29 SLN-negative and 6 SLN-positive patients), or on a selective basis, when an SLN was found to be positive (72 patients). ALND was neither performed on a selective basis when the SLNs were negative, nor when the patient was randomised in the European Organisation for the Research and Treatment of Cancer study comparing ALND versus axillary radiotherapy for SLN-positive patients (after mapping of the axilla: radiotherapy or surgery – AMAROS) (4 patients), nor when the patients wished not to have this intervention (7 patients, one of them with severe comorbidities; and 6 further patients with only isolated tumour cells (ITC) in the SLN). The date of introduction of SLNB differed from institution to institution, but the patients were operated on between November 1997 and August 2006 in the institution with the longest series; most centres entered data from operations performed between 2000 and 2005.

The pathological analysis of the SLNs was not uniform either, but a multilevel assessment with haematoxylin and eosin (HE) staining was used for all SLNs in all the participating pathology departments. Larger SLNs were halved or sliced into several parallel pieces. SLNs negative on gross or intraoperative assessment were subjected to step-sectioning at intervals of 100–500 μm, depending on the department; a minimum of three deeper levels were examined in all such cases. Cytokeratin immunohistochemistry was used for HE-negative cases in 452/477 (94.8%), and was not performed in 24 HE-negative cases, depending on the institutional protocol. Non-SLNs were assessed by single or multiple levels (for larger lymph nodes) stained by HE.

Whenever there were multiple tumours or multiple foci of tumour in the breast, the largest tumour size was entered in the analysis, in keeping with the pT classification of malignant tumours in the tumour-node-metastasis (TNM) system.[14] In cases of multiple tumours, a histological type other than those specified above resulted in exclusion of the case from the analysis. For the purpose of this study, any tumour cell in an SLN was considered a positive finding. The nodal involvement was then categorised into ITCs, micrometastases (larger than 0.2 mm, but not larger than 2 mm) or macrometastases (larger than 2 mm) according to the definitions of these categories.[14–16] In an earlier study, our group demonstrated that the separation of ITCs from micrometastases was less than optimal, but the reproducibility could be improved by following some agreed criteria in keeping with the general rules of the TNM classification of malignant tumours.[14,15] Participants tried to adhere to these criteria,[10,17] along with the definitions[14,15] in order to improve the reproducibility of nodal staging.

The data collected on each case included the patient's age, the tumour type, the invasive component size and grade, the absence or presence of lymphovascular invasion (LVI), the number of SLNs removed and involved, the pN category of the SLN involvement (negative versus ITC versus micrometastasis versus macrometastasis), the presence or absence of extracapsular spread in positive SLNs, whether ALND was performed or not, and the number of non-SLNs removed and metastatic. Gender was not considered in this study, because SLNB is feasible in clinically node-negative male breast cancers, and furnishes results comparable with those obtained on large series of female breast carcinomas; accordingly, a few male breast cancer cases might have been mixed with the overwhelming majority of female carcinomas in this study.

Univariate analysis for categorical data was performed with the chi-square test, whereas for continuous variables it was carried out by using univariate logistic regression. Multivariate analysis comprised logistic regression and stepwise multiple regression with backward and forward selection. The analyses were achieved with the OS4 statistical software.[18]

3. Results

The study involved 572 breast carcinoma cases of special types with a favourable prognosis. Details on the studied cases are presented in Table 1. Most of the tumours were of the tubular/cribriform type, and were grade I tumours. Carcinomas with a higher histological grade were of the mucinous or papillary types.

The frequencies of SLN positivity according to the different values of the categorical variables are shown in Table 2, which also includes the results of the univariate analyses relating to the listed variables. The factors significantly associated with SLN involvement were the presence of LVI, the tumour size, the tumour type, the number of SLNs removed and the focality (multiple versus unifocal). The same variables were found to be the independent variables predicting SLN involvement by logistic regression (Table 3). The backward and the forward stepwise multiple regression yielded similar results, and implicated the same variables. When ITCs were considered a negative finding, as suggested by the pN0(i+) category of the TNM system,[14–16] the focality proved not to be significant in either the univariate or the multivariate approach.

Table 1 – Basic characteristics of the tumours (patients) analysed

Mean (±SD; range) age of the patients (years)	59 (±11; 26–89)
Median (mean ± SD; range) tumour size for all tumours	10 mm (11.2 ± 5.4; 0–45)
Tumour sizes as pT categories	
pT1a	56 (9.8%)
pT1b	246 (43.0%)
pT1c	239 (41.8%)
pT2	31 (5.4%)
Combined histological grade (Nottingham)	
Grade I	490 (85.7%)
Grade II	68 (11.9%)
Grade III	14 (2.4%)
Invasive tumours by type	
Tubular/cribriform carcinomas	427 (74.7%)
Mucinous carcinomas	114 (19.9%)
Papillary carcinomas	31 (5.4%)
Focality of the tumours	
Unifocal tumours	510 (89.2%)
Multiple tumours (multifocal or multicentric)	54 (9.4%)
Tumours with no data on focality	8 (1.4%)
Lymphovascular invasion in the primary tumour	47 (8.2%)
1/2/3/4/5/6 SLNs removed per patient	290/173/70/23/15/1
Median (mean ± SD; range) of SLNs removed per patient	1 (1.8 ± 0.4; 1–6)
SLN involvement (by ITC/micrometastasis/macrometastasis)	95 (16.6%) (10/48/37)
Extracapsular extension of SLN metastasis	12 (12.6%)
All patients with ALND	107 (18.7%)
SLN-positive patients with ALND	78 (82.1%)
Median (mean ± SD; range) of non-SLNs removed per patient with ALND	14 (14.9 ± 7; 3–36)
All non-SLN positive patients	21 (3.7%)

SLN: sentinel lymph node; ITC: isolated tumour cells; ALND: axillary lymph node dissection.

Tumours belonging in the pT1a (not larger than 5 mm) or pT1b (larger than 5 mm but not larger than 10 mm) categories were associated with overall 3.6% and 10.2% SLN metastasis (ITC excluded), but when analysed by mm size categories, tumours measuring 10 mm in greatest dimension displayed 17.9% (12/67) SLN involvement, and those measuring 8 and 9 mm also had relatively high incidences of SLN positivity (5/51 and 6/52, respectively). When the lack of LVI was also considered, pT1a and pT1b carcinomas exhibited SLN metastasis in portions of 3.7% and 8.4%, respectively. When analysed mm by mm, tumours smaller than 10 mm had less than 10% SLN involvement, whereas those reaching 10 mm were SLN-positive in 13.1%, and all larger tumours also had >10% SLN involvement. As shown in Table 1, mucinous carcinomas had 7% SLN metastasis. Patients without LVI and with 1 SLN identified had a 22/264 (7.6%) metastasis rate in these lymph nodes, whereas those with more than 1 SLN removed had a metastasis rate of 39/261 (14.9%). Tumours belonging in the pT1a and pT1b size categories, without LVI and only 1 SLN identified, had low rates (4%) of SLN positivity: 1/25 and 5/121, respectively, whereas larger tumours with the same features had >10% SLN positivity. The combination of these three factors into the worst profile (i.e. the presence of LVI, a tumour larger than 10 mm, and more than 1 SLN removed) had a high incidence of SLN involvement (7 macrometastases and 5 micrometastases out of 19 carcinomas; 63.2%).

As concerns the 107 patients who underwent axillary lymph node dissection, the involvement of non-SLNs was found in 21 (3.7% of all patients, and 19.6% of all patients with axillary dissection). Two of the non-SLN positive cases were patients with negative SLNs, who were therefore interpreted as false-negative SLN biopsy cases. The factors bearing on the frequency of non-SLN involvement are shown in Table 4. None of the variables found to be significant in the univariate analysis proved significant in the logistic regression. When the forward and backward stepwise multiple regressions were also performed, LVI ($p = 0.025$) and the proportion of positive SLNs ($p = 0.019$) were found to be significant.

When only the 78 patients who had positive SLNs and axillary dissection were considered, the non-SLN metastasis rate was higher for tumours which had LVI identified (11/26; 42.3%) than for tumours without demonstrated LVI (8/52; 15.4%). In the latter category, patients at the lower end of the SLN ratio values (for practical purposes the cases were divided into the two categories of up to or more than 50% of the SLNs found positive) had a lower non-SLN involvement rate (2/26; 7.7%) than those at the top end (6/26; 23.1%). Of the patients who had both LVI and a positive SLN ratio above 50%, the rate of non-SLN involvement was the highest (8/17; 47.1%).

Table 2 – Frequency of SLN involvement according to the variables analysed, and the results of the univariate analyses

Variable	SLN+ (ITC incl)/All	*p*	SLN+ (ITC excl)/All	*p*
Age		0.589		0.6466
Tumour size		<0.001		0.0001
Number of SLNs		0.028		0.0895
Histological type		0.020		0.029
Tubular/cribriform	80/427 (18.7%)		71/427 (16.6%)	
Mucinous	9/114 (7.9%)		8/114 (7.0%)	
Papillary	6/31 (19.4%)		6/31 (19.4%)	
Grade		0.884		0.733
Grade 1	81/490 (16.5%)		73/490 (14.9%)	
Grade 2	11/68 (16.2%)		5/59 (15.3%)	
Grade 3	3/14 (21.4%)		3/14 (21.4%)	
LVI		<0.001		<0.001
LVI present	27/47 (57.4%)		26/47 (55.3%)	
LVI absent	68/525 (13.0%)		59/525 (11.2%)	
Focality		0.003		0.006
Unifocal	78/510 (15.3%)		70/510 (13.7%)	
Multifocal	17/54 (31.5%)		15/54 (27.8%)	

SLN: sentinel lymph node; ITC: isolated tumour cells; LVI: lymphovascular invasion.

Table 3 – Multivariate (logistic regression) analysis of the factors influencing SLN involvement

Variable	O.R.	95% CI	p	O.R.	(95% CI)	p
(A) *ITC included as SLN+*						
Focality	2.2107	1.1045–4.4249	0.0250	2.0630	1.0447–4.0739	0.0370
Grade	1.1453	0.5020–2.6133	0.7471	–	–	–
Number of SLNs	1.3484	1.0798–1.6838	0.0084	1.3231	1.0628–1.6473	0.0123
Tumour size (mm)	1.0707	1.0238–1.1198	0.0028	1.0725	1.0261–1.1209	0.0019
Type	0.3808	0.1849–0.7839	0.0088	0.4421	0.2602–0.7512	0.0025
LVI	10.5282	4.9472–22.4053	<0.0001	9.3753	4.5771–19.2037	<0.0001
Age (years)	1.0185	0.9952–1.0423	0.1199	–	–	–
(B) *ITC excluded from SLN+*						
Focality	2.0249	0.9795–4.1858	0.0569	–	–	–
Grade	0.9209	0.3951–2.1466	0.8487	–	–	–
Number of SLNs	1.3001	1.0281–1.6439	0.0284	1.2722	1.0122–1.5990	0.0390
Tumour size (mm)	1.0794	1.0307–1.1304	0.0012	1.0794	1.0317–1.1294	0.0009
Type	0.4520	0.2205–0.9269	0.0302	0.4602	0.2685–0.7887	0.0047
LVI	11.0285	5.1677–23.5365	<0.0001	10.4525	5.1775–21.1015	<0.0001
Age (years)	1.0184	0.9942–1.0432	0.1382	–	–	–

SLN: sentinel lymph node; ITC: isolated tumour cells; LVI: lymphovascular invasion.

Of the 13 patients who had positive findings (including ITCs) in the SLN but no axillary treatment (surgery or radiotherapy), 2 were lost to follow-up, the remaining 11 have no evidence of disease after a median follow-up of 33 months (range: 18–83 months).

4. Discussion

Some kind of surgical and pathological axillary staging is generally performed in breast cancer patients, and the information acquired is used as a key factor in determining the need for adjuvant systemic treatment, in choosing between different systemic treatment options and in recommending radiotherapy, especially postmastectomy radiotherapy. The traditional staging intervention was ALND. However, some studies have reported that a wait-and-see policy can also be acceptable in some patients with a low expected risk of nodal metastases.[3,4,19] These studies indicate that the rate of axillary recurrences is generally low at 10 years, and is tumour size-dependent. Salvage ALND can be performed without extra morbidity and with acceptable disease control.[3,19] SLNB has now become a standard staging procedure for clinically node-negative breast carcinomas. However, the debate is continuing as to whether this low, but not zero-morbidity intervention should be offered to everyone with breast cancer. The controversy pertaining to the management of the axilla generated a national one-day debate in the United Kingdom on 8th September 2005, when Benson suggested that observation alone may be an acceptable approach, for example in patients with a low (5–10%) risk of nodal involvement, because this is the reported false-negative rate of SLNB; these patients are those with small tumours and a favourable histological grade.[20] In the present study, we tested whether favourable histologic types, i.e. tubular/cribriform, mucinous and papil-

Table 4 – Frequency of non-SLN involvement according to the variables analysed, and the results of the univariate analyses

Variable	Non-SLN+/All ALND	p
Age		0.316
Tumour size		0.024
Number of SLNs		0.202
Number of positive SLNs		0.022
SLN+ ratio		0.003
Histological type		0.101
Tubular/cribriform	14/86 (16.3%)	
Mucinous	6/15 (40%)	
Papillary	1/6 (16.7%)	
Grade		0.334
Grade 1	16/91 (17.6%)	
Grade 2	4/11 (36.4%)	
Grade 3	1/5 (20%)	
LVI		0.002
LVI present	11/28 (39.3%)	
LVI absent	10/79 (12.7%)	
Focality		0.120
Unifocal	16/90 (17.8%)	
Multifocal	5/14 (35.7%)	
pN(sn)		0.002
pN0(i–)	2/29 (6.9%)	
pN0(i+) (ITC)	1/4 (25%)	
pN1mi (micrometastasis)	4/39 (10.3%)	
pN1 (macrometastasis)	14/35 (40.0%)	
EC spread		1.000
Absent	16/66 (24.2%)	
Present	3/12 (25%)	

SLN: sentinel lymph node; ITC: isolated tumour cells; LVI: lymphovascular invasion; ALND: axillary lymph node dissection; EC: extracapsular.

lary carcinomas, could have implications as concerns the indication of SLNB or ALND after the finding of positive SLNs.

SLNB has a recognised false-negative rate ranging from 5% to 10%.[7] Whenever SLNB is used to tailor the management of the axilla, this range of errors must be accepted; accordingly, a maximum of 10% missed nodal positivity was considered acceptable in the present work. It should also be borne in mind that not all axillary metastases become clinically evident,[1] and false-negatively staged patients may not obviously derive a prognostic disadvantage from this false staging.

The first analysis demonstrated that SLN involvement (including ITCs) was associated with lymphovascular invasion, a larger tumour size, the tubular or papillary type, more SLNs identified and multifocality. Although debate is continuing as to the therapeutic implications of the finding of ITCs in the SLNs, these low volume nodal findings are generally not considered metastasis from the aspect of staging and treatment planning,[2,21,22], in keeping with the TNM classification.[14–16] The analysis was therefore also performed after exclusion of the ITCs from the node-positive category. The same variables, except focality, were associated with SLN involvement.

These results are in keeping with those of a large single institutional study, where tumour size and LVI were the two most important predictors of SLN involvement, and favourable histological types also influenced the rate of SLN metastasis.[23] The University of Louisville Breast Cancer Study Group also assessed the frequency of SLN metastases in connection with the special type cancers analysed here[24]: tubular and mucinous carcinomas were found to have similar rates of SLN involvement to those observed in our study (17% and 6%, respectively), whereas papillary carcinomas displayed a lower rate of SLN disease in the Louisville study: 7% versus 19%. This difference may perhaps be explained by the fact that papillary carcinomas do not form a homogeneous histological group. They encompass in situ carcinomas (used synonymously with intraductal papillary carcinoma),[25] invasive carcinomas with a predominant papillary pattern and invasive carcinomas of no special type arising in the setting of intraductal or intracystic papillary carcinomas.[26]

The data from before the SLNB era support the notion that a subgroup of patients can be identified with a nodal metastasis rate smaller than 10%. When analysing the 12,950 tumours not larger than 10 mm in the Survival Epidemiology and End Results database, Maibenco and colleagues found an overall rate of 3.9% of nodal metastasis in tumours of favourable histological type. This contrasted with the 13.9% rate of node positivity for the other types.[27] A meta-analysis of the frequency of nodal metastasis in tubular carcinomas suggested a 6.6% rate for pure tubular carcinomas.[28] The lower rates from these earlier studies may probably be explained by the fact that the SLN are often subjected to more scrutiny than lymph nodes in general, and more metastases can be identified in them. This is reflected by the fact that a majority of the metastases found belonged in the micrometastatic category (Table 1).

As suggested above, the tumour size and LVI were identified earlier as factors influencing nodal, or more specifically SLN metastasis, and focality was also implicated in some series.[29,30] The only contradictory factor emerging from our analysis is the number of SLNs. It might be inferred that this factor simply reflects a statistical chance of randomly finding a metastasis: the examination of more SLNs leads to a greater possibility of finding a positive SLN, similarly as in nodal staging in general,[31,32] and a single SLN removed during lymphatic mapping was found to be associated with higher rates of false negativity.[33] If this were true (and this area requires further study), a single SLN recovered from the axilla would indeed be associated with a lower detected metastasis rate, but not with an actual lower metastasis rate.

Whenever an SLN is found to be metastatic, the current standard treatment involves ALND,[2] although it is acknowledged that such an approach may result in the overtreatment of about 60% of the patients, or even 75% in women with a low risk of nodal involvement, such as those reported here. It is important to identify patients with a low likelihood of exhibiting further nodal involvement in the axilla, because they could be offered a wait-and-see policy instead of undergoing ALND and being exposed to its morbidity. A recent meta-analysis identified five factors which significantly influence the rate of non-SLN metastases: the size of the SLN metastasis, the extracapsular extension of the SLN involvement, the number of SLNs involved, the primary tumour size and the presence of LVI.[34] The univariate analyses in our study identified four of these factors as being significantly associated with non-SLN involvement. Extracapsular extension was rather rare with these tumours, and this may have accounted

for the similar rates of non-SLN metastasis when this phenomenon was present or absent. The multivariate analysis highlighted only two independent factors that were significantly associated with non-SLN involvement: LVI and the proportion of involved SLNs.

Although the theoretical possibility of haematogenous lymph node metastasis cannot be excluded, LVI must be regarded as an obligatory predecessor of nodal metastasis, because the tumour cells reach the SLNs via the lymphatic vessels. However, LVI is not always seen when nodal metastases are present (11% in this series), a situation that is simply explained by the fact that the histopathological assessment is based on sampling. LVI may be too minuscule as a change to be included in the tissue blocks: it may either be seen by chance in the sectioning level examined, or it must be extensive to be detected by random sampling. The latter occurrence certainly harbours a much higher chance of nodal metastasis and may be the explanation of why LVI is associated not only with the presence of metastatic SLNs, but also with metastasis to non-SLNs.

The other variable, the proportion of involved SLNs, reflects the nodal metastatic load as the ratio of positive SLNs and all SLNs removed. Several studies have included the number of positive SLNs in their analysis of the risks of non-SLN involvement, and have found it to be a significant predictor.[24,34–37] However, it is not indifferent whether a metastatic SLN is one of 3–4 SLNs removed or a single one. Likewise, the numbers of negative SLNs or all SLNs removed have been reported to be significant variables influencing the rate of non-SLN metastasis .[38–40] A few investigations have even used the percentage or ratio of the affected SLNs, and this derived variable also proved useful in the prediction of non-SLN involvement[41–44] or massive axillary nodal involvement.[45] Besides the SLN setting, the lymph node ratio (LNR) was found to be a better prognosticator in breast cancer than the number of involved lymph nodes, which is generally considered to be the single most important prognostic factor of this disease.[46,47] The Nottingham prognostic index, derived from the tumour size, the histological grade and the nodal stage, was outperformed by the LNR-based prognostic index, where the nodal stage was substituted by an LNR-based score.[48]

As concerns the other factors which have often been found to be associated with metastases in non-SLNs, the sizes of the primary tumour and of the SLN metastasis might have failed to be significant in the subset of patients analysed here because the majority of the tumours were small and of low grade. Low case numbers may also have influenced the results, but it is more likely that these factors have less bearing on the incidence of non-SLN metastases than do LVI and the extent of the nodal load, as reflected by the positive SLN ratio. The present series included relatively high numbers of these tumours, but both SLN involvement and more explicitly non-SLN involvement were rare.

Although the special types of carcinoma investigated generally have a good prognosis, they may be associated with considerable rates of overall nodal involvement. It should be borne in mind that when the factors influencing nodal involvement accumulate as a poor combination, the rate of SLN involvement may be too high to allow a conservative wait-and-see policy. On the other hand, our results suggest that when tumour size is small (pT1a and pT1b), LVI is absent and only 1 SLN is identified, the risk of SLN (or lymph node) involvement is in the range of the false-negative rate of SLN biopsy (less than 10%), and probably allows the approach of observation alone instead of a surgical staging procedure.

When SLNB is performed in these low-risk, special type carcinomas, the finding of a metastasis poses a second uncertainty about the need for a completion ALND. Again, the identification of factors influencing non-SLN involvement can help in the identification of patients with a low possibility of further nodal metastasis, such as those who lack LVI and have a low SLN ratio (up to 50%), and in whom the omission of ALND may be a reasonable alternative approach. Additionally, the opposite end of the spectrum may be suggested. When the relevant factors accumulate to form a poor predictive profile (LVI present and positive SLN proportion above 50%), ALND may be considered a requisite, because of the association with the greater than 50% rate of non-SLN involvement. This study is probably the first to highlight this end of the spectrum.

The types of breast carcinomas analysed here may have a favourable prognosis even in the presence of lymph node metastasis.[5] Our results highlight the view that some patients may not even require SLNB for staging, and others can be candidates for the omission of completion ALND when an SLN is found to harbour metastasis.[49] On the other hand, high risks of SLN metastasis and non-SLN involvement may indicate SLNB followed by ALND even in these tumours with a favourable outcome.

Note added in proof

In support of our findings related to the lack of association between non-SLN metastases and extracapsular spread of SLN metastasis in this set of tumours, it has been reported that extracapsular extension of SLN micrometastases are seen predominantly in tubular carcinomas, and may possibly be of less disadvantage than extracapsular spread in general.[50]

Conflict of interest statement

None declared.

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