Review Article

Predictive Factors of Lymph Node Involvement in the Surgical Management of Breast Cancer: Retrospective Study and Literature Review

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Abstract

Introduction: Breast cancer is the leading women's cancer, with 49,814 new cases per year in France in 2005 (36.7% of new cancer cases), and the leading cause of women's mortality with cancer [1]. Axillary node status is a major prognostic factor in breast cancer affecting overall survival and recurrence after treatment.

Objectives: To elucidate the relationship between the various clinical and anatomopathological characteristics of breast cancer and axillary node invasion, to reduce the number of axillary curage procedures performed and to propose the use of the sentinel lymph node technique more and more.

Material and method: *Descriptive and analytical retrospective study about 96 cases of breast cancer have benefited from a first surgery within the service of gynecology obstetrics I of the CHU Hassan II of Fez, Morocco.*

Results*: According to our study and the data found in the literature, we were able to highlight the existence of predictive factors of GG invasion in the case of complete axillary curage: the histological size of the primary tumor, the initial location in the SOQ (super outer quadrant of the breast), the lobular histological type, the high SBR grade, also a high KI67 and the HER2 IHC profile. We also found that a negative predictive factor was the absence of adenopathy on clinical examination and axillary ultrasound.*

Conclusion*: For several years, the axillary curage is no longer recommended because of its complications, the method of the sentinel lymph node became the reference in the management of breast cancer, the goal of our study is to encourage to practice this method more and more and to widen or adapt its indication according to our context.*

Keywords*: Breast cancer, palpable lymph node, histological size, vascular emboli, sentinel node.*

Introduction

Breast cancer is the leading women's cancer, with 49,814 new cases per year in France in 2005 (36.7% of new cancer cases), and the leading cause of cancer mortality in women: 11,201 deaths per year in France in 2005 (17.7 per 100,000) **[1]**.

The status of the axillary lymph nodes is a major prognostic factor in breast cancer, affecting overall survival and recurrence after treatment: lymph node dissection is the reference for assessing their invasion but at the cost of significant morbidity **[**2, 3**]**.

Currently, the sentinel node technique has become an essential method in the diagnosis and treatment of localized breast cancer, which offers several advantages, in particular the reduction of complications related to axillary curage. It is rarely used in our context, due to the lack of an adequate technical platform or a lack of clinical indication.

Material and method

We conducted a retrospective descriptive and analytical study of 96 cases of breast cancer managed in our training and have benefited from a first surgery in the department of gynecology-obstetrics I of HASSAN II university hospital, Fez, Morocco.

Our main objective was to highlight the relationship between the different clinical and anatomopathological characteristics of breast cancer on the one hand and axillary lymph node invasion, on the other hand, to deduce the predictive factors of lymph node invasion and thus to reduce the number of axillary curage done and to propose to reinforce the place of the sentinel lymph node technique in our practice.

Results

we retained 96 files of patients who had undergone primary surgery for breast cancer, of which 60 patients had secondary lymph node involvement. we studied the different clinical, radiological and anatomopathological aspects, which we will detail in this paper.to determine a causal relationship between the different factors and the occurrence of lymph node involvement we studied for each factor the chance of occurrence or percentage of occurrence, the relative risk and the odds ratio.

In our serie, the average age is 51 years with extremes of 32 and 77 years with a clear predominance of 40-49 years. 60 patients out of 96 presented lymph node metastases at the final anatomopathological study, the percentage of which is 62.5%.

According to hormonal status, we noted an equal distribution, 48 patients in genital activity had no lymph node involvement, and 48 patients who had already reached menopause had positive lymph node involvement on the final anatomopathological study. In addition, we did not take into consideration the notion of taking oestroprogestative contraception or hormone replacement therapy because of the lack of data in the files.

Topographically, It can be seen that the most common location is the upper external quadrant region, which was found to be 50% in patients with no lymph node involvement and 58.33% in patients with secondary lymph node involvement.

Regarding tumor size in patients with lymph node metastases, there was a clear predominance of tumors larger than 5 cm (T3) in 73.33% of patients with secondary lymph node involvement, and overall involvement of 45%,8%.

In addition, among the patients without lymph node involvement, 2 patients had a tumor of less than 2 cm (T1), 23 patients had a tumor between 2 cm and 5 cm (T2), and 11 patients had a tumor of more than 5 cm (T3). Graph 1 shows the distribution of lymph node involvement by clinical tumoral size.
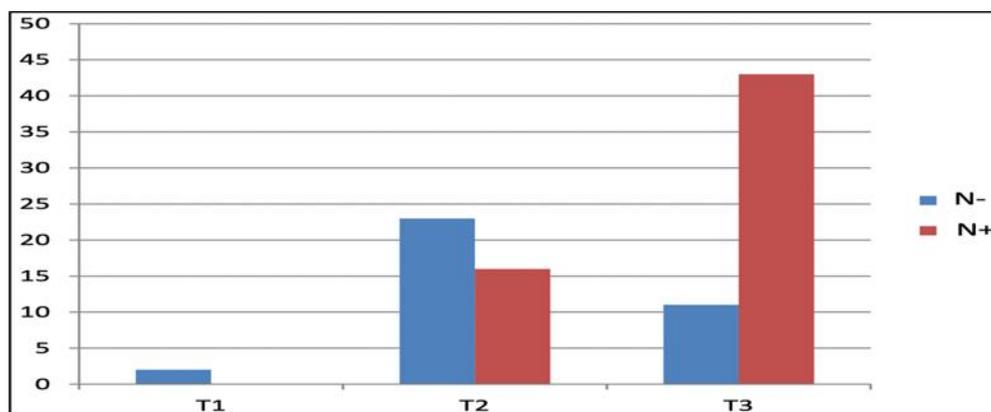
Graph1: distribution of lymph node involvement by clinical tumoral size

The clinical examination of the axillary hollow showed that in patients without lymph node involvement only 3 patients had a palpable lymph node on examination with a percentage of 8.33%. However, in patients with lymph node metastases, 43 patients had a palpable node on clinical examination, representing 71.6% of this group.

On the paraclinical level, all our patients had undergone a breast ultrasound and mammography. All patients underwent a breast ultrasound and a mammogram, as well as an extension test, which was negative.

At the breast ultrasound/mammography only 21.87% of the patients had suspected ACR4 lesions, and 78.13% had ACR5 lesions.

Concerning the ultrasound of the axillary hollow, there was a strong correlation between the identification of adenopathy on ultrasound and its involvement in anatomopathological examination.

In patients without lymph node involvement, only 6 patients had axillary adenopathy on ultrasound and therefore a percentage of 16.66% of false positives. In patients with lymph node metastases, only 12 patients had no axillary adenopathy on ultrasound and therefore a false negative rate of 20%.

In our serie, the overall sensitivity of axillary ultrasound is 80% and the specificity of this examination is 83.33%. It can be concluded that the data of the axillary ultrasound are reliable with fairly high sensitivity and specificity concerning secondary lymph node involvement.

All patients included in our study underwent diagnostic micro biopsy, with the following anatomical-pathological findings:

- the predominant histological type in our serie is infiltrating ductal carcinoma in 92 patients, and only 4 patients had an infiltrating lobular type, all of which had secondary lymph node involvement.

- The distribution of patients in the two groups (with and without lymph node involvement) was homogeneous according to SBR grade.

	N- (n,%)	N+ (n,%)
SBR1	**3/8.33%**	**3/5%**
SBR2	**25/69.44%**	**37/61%**
SBR3	**8/22.22%**	**20/33.33%**

Table 1: Distribution by SBR grade.

- Concerning vascular emboli, in our serie there was a strong correlation between the absence of vascular emboli and the absence of lymph node involvement, of the 36 patients without lymph node involvement only 3 had vascular emboli, with a 91.66% chance of not having definitive lymph node involvement if there are no vascular emboli on biopsy. However, the presence of vascular emboli in the 60 patients with lymph node involvement was quantified in only 14 patients with an odds ratio of 0.019, demonstrating that there is no direct relationship between the presence of vascular emboli and the presence of secondary lymph node involvement.

- the immunohistochemical profile:

  o In the group of patients without lymph node involvement, 24 had positive hormone receptors and 46 in the group of patients with lymph node involvement. 73.87% of the patients in our serie had hormone-sensitive cancer.

  o Concerning HER2 gene overexpression, it was found in 12 patients in the group with lymph node involvement and only in 3 patients without lymph node involvement. Thus, we can conclude that in our serie only the HER2 profile is not significant for lymph node invasion.

  o We also looked for the Ki67 score, which we considered high if it was above 20% according to the Ki67-recoGE recommendations. We note that there is a strong correlation between the high KI67 score and the presence of lymph node metastasis with a high risk of 73.33% and an Odd ratio of 3.77 which is highly significant.

- We also looked at the distribution of our patients according to the general IHC profile and therefore on 4 categories, the following graph 2 shows the distribution of lymph node involvement by IHC profile:

It can be clearly seen that the HER2 profile is strongly implicated in the occurrence of lymph node metastasis with a rate of 100% in our serie.
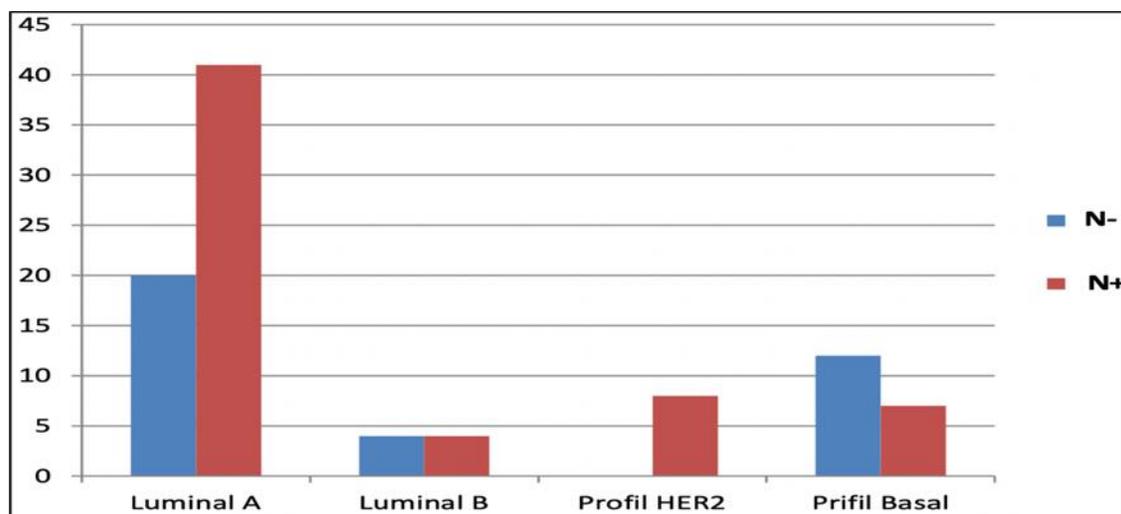
Graph 2: Distribution of lymph node involvement by IHC profile

In the following table, we have compared ́the majority of the collected data studied by most authors, who performed a statistical test based on the Odd Ratio also called close relative risk, it's a statistical measure, often used in epidemiology, expressing the degree of dependence between qualitative random variables. An odd ratio:

- < 1 means that the event is less frequent in group A than in group B;

- = 1 means that the event is equally frequent in both groups;

- > 1 means that the event is more frequent in group A than in group B.

We thus calculated ́the relative risk of the occurrence of lymph node metastases in both groups:

Variable studied	N- (Number of patients (and %))	N+ (Number of patients (and %))	Odd ratio	Risque relatif
Number of patients	36	60	-	-
Age (years old): **<50** **>50**	18(50%) 18(50%)	27(45%) 33(55%)	0,81 1,22	0,24 0,22

Histologic tumor size (mm):	.	.	.	.
T1	2(5,5%)	0(0%)		
T2	23(63,9%)	16(26,6%)	0,17	0,32
T3	11(30,5%)	44(73,3%)	5,75	3,04
Histologique type:				
Ductal	36(100%)	56(93%)		
Lobular	0(0%)	4(7%)	100%	
SBR histologic grade:				
1	3(8,3%)	3(5%)		
2	25(69,4%)	37(61,6%)	0,59	0,42
3	8(22,2%)	20(33,3%)	1,68	2,34
Estrogen receptors :				
-	24(66,6%)	14(23,3%)	0,15	1,42
+	12(33,3%)	46(76,6%)	6,58	2,15
Progesteron receptors :				
-	24(66,6%)	14(23,3%)	0,15	1,42
+	12(33,3%)	46(76,6%)	6,58	2,15
Emboles vasculaires :				
-	33(91,6%)	46(76,6%)	0,47	3,34
+	3(8,3%)	14(23,3%)	2,12	0,29
High KI67 score:				
Yes	23(63,8%)	16(26,6%)	0,2	0,31
No	13(36,1%)	44(73,3%)	4,84	3,15
HER2 score:				
-	33(83,9%)	48(80 %)	2,75	0,47
+	3(16,1%)	12(20%)	0,36	2,1

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Profil IHC :				
Luminal A	20(55,5%)	41(68,3%)	1,23	
Luminal B	4(11,1%)	4(6,6%)	0.6	
HER2	0(0)	8(13,3%)	100%	
Triple negatif	12(33,3%)	7(11,6%)	0,35	

Table 2: Overall statistical statement of our serie:

Discussion:

In this study, we showed that 62.5% of our patients had lymph node invasion after axillary curage in the management of their breast cancer.

We found that the size of the primary tumor, the histological type and the presence of vascular emboli were statistically significant predictors of lymph node invasion in the axillary cavity. We will detail the different factors investigated in this study as follows:

Clinical characteristics:

The age of the patient did not appear to be a predictive factor of GG invasion in our study, which was consistent with the vast majority of studies.

Tumor location, a variable investigated in our study, showed that the presence of the primary tumor in the SOQ (super outer quadrant of the breast), is strongly related to the presence of metastatic axillary GGs, this factor has never been reported in the literature as an independent risk factor for lymph node involvement.

Initial tumor size: As in our study, the size of the tumor was found to be a predictive factor of lymph node involvement, we noted a high probability of lymph node involvement if the size was greater than 5 cm (T3) with an Odds Ratio of 5,75.

In the majority of studies: Barranger et al. report a 0% risk of lymph node involvement if the tumor is less than 10 mm, a 17% risk if it is between 11 and 20 mm and a 67% risk if it is more than 20 mm [4]. Nos et al. also report that a tumor size greater than 20 mm is predictive of lymph node involvement [5], as have many other authors [6, 7]. In our study, the probability of involvement if the size is less than 2 cm is 0%, and very low if T2.

Clinical and ultrasound exploration of the axillary fossa:

In our study we found ´a strong correlation between the absence of GG on clinical examination and the absence of affected GG on pathological examination, with a 91.66% chance of not finding an affected GG.

Concerning the radiological exploration of the axillary cavity, our study showed that the presence of adenopathy on ultrasound is related to the involvement of lymph nodes after curage with a chance of 80% of invasion. The specificity of ultrasound is 83.3%. The majority of studies did not mention these two factors in their analysis.

Histological characteristics:

The histological type of the primary tumor was found to be a predictive factor for lymph node invasion with a rate of 100% in the case of infiltrating lobular carcinoma, but this histological type was only found in 4 patients in our serie. This factor has not been approved in the literature, so there does not seem to be more lymph node involvement in cases of infiltrating lobular carcinoma [8].

In our study, the SBR grade analysis did not show a relationship between histopronostic grade and lymph node involvement.

These data are consistent with those found in the literature, Only Goyat et al. found ´a significant association between SBR grade and GG invasion with a risk of less than 50% if SBR2 and very high risk at 76.3% if SBR3 [9].

In our study, the presence of lymphovascular emboli did not appear to be an independent risk factor for lymph node involvement, but the absence of vascular emboli at biopsy was strongly associated with the absence of lymph node involvement with a rate of 91.6%. The results found in the literature are divergent: if Chu [7],

Houvenaeghel [10] for example had identical results to ours, several studies, including Viale [11] and Sachdev [12] reported the presence of lymphovascular emboli as an independent risk factor for lymph node involvement.

The only serie found that studied the relationship between lymph node involvement and hormone receptors as well as HER2 and KI67 status is the serie of Abdessalam SF and co [13] who did not find an obvious relationship.

However, in our serie, the risk of lymph node involvement is multiplied by 3,7 if the KI67 score is high and the chance of involvement is 73.3%.

Isolated analysis of hormone receptors and HER2 profile did not show a direct relationship between their presence and lymph node involvement, however, combined analysis of these factors showed a strong correlation between HER2 profile (+ negative hormone receptors) and lymph node involvement with a 100% risk (only 8 cases).

Conclusion

According to our study and the data found in the literature, we were able to highlight the existence of predictive factors of GG invasion in the case of complete axillary curage: the location in the QSE, the initial histological size of the primary tumor, the lobular histological type, the high SBR grade, also a high KI67 and the HER2 IHC profile.

Also, we have highlighted the existence of a negative predictive factor which is the absence of adenopathy on clinical examination and ultrasound of the axillary cavity.

For several years, the axillary curage is no longer recommended because of its complications, the method of the sentinel node became the reference in the management of breast cancer, the purpose of our study is to encourage to practice this method more and more and to widen or adapt its indication according to our context.

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