

Predictors of Lymph Node Metastases in Breast cancer

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Introduction

- Axillary lymph node involvement is one of the most important prognostic factors in patients with breast cancer.
- However the most appropriate level of axillary dissection for breast cancer remains unclear.
- The use of sentinel lymph node biopsy has been shown to be associated with reduced risk of lymphedema and shoulder stiffness.
- In selected cases with minimal risk of lymph node involvement, axillary dissection can be omitted; however there is a risk of understaging the axilla and hence undertreating the woman with breast cancer.

Clinical and intraoperative assessment of axillary lymph nodes

- A prospective study was carried out in the University Malaya Medical Centre over a 6 month period from April to Oct 2005, where clinical examination of the tumour size and axilla, and intra-operative assessment of axilla was correlated with pathological examination of the size of the tumour and lymph nodes involvement.

Harun NH, Taib NA, Yip CH. Is clinical assessment of the axilla a reliable indicator for lymph node metastases in breast cancer? ANZ J Surg 2008 Nov;78(11):943-4.

Results

- 110 women with operable T1-3, N0-1 breast cancer was recruited into this study. 31 patients (28.9%) had breast conservation surgery while 79 patients had mastectomy and axillary dissection.
- 53 patients (48.2%) were node positive with a range of 1-26 lymph nodes Out of the 53 patients with nodes involved, only 24 patients had clinically palpable nodes (Sensitivity 45.3%).

Results

- However out of the 29 patients with clinically palpable nodes, only 5 turned out not to have involved nodes (specificity 91.2%).
- Intraoperative palpation was more sensitive – out of the 53 patients with involved nodes, 43 were positive by intraoperative palpation (sensitivity of 81.1%). However intraoperative palpation was less specific; out of the 61 patients where the surgeon intra-operatively felt that nodes were involved, 18 turned out to be node-negative, giving a specificity of 68.4%.

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Conclusion

- Clinical and intraoperative evaluation of the axilla is inaccurate, requiring at least a Level 1-2 dissection of the axilla in all cases.

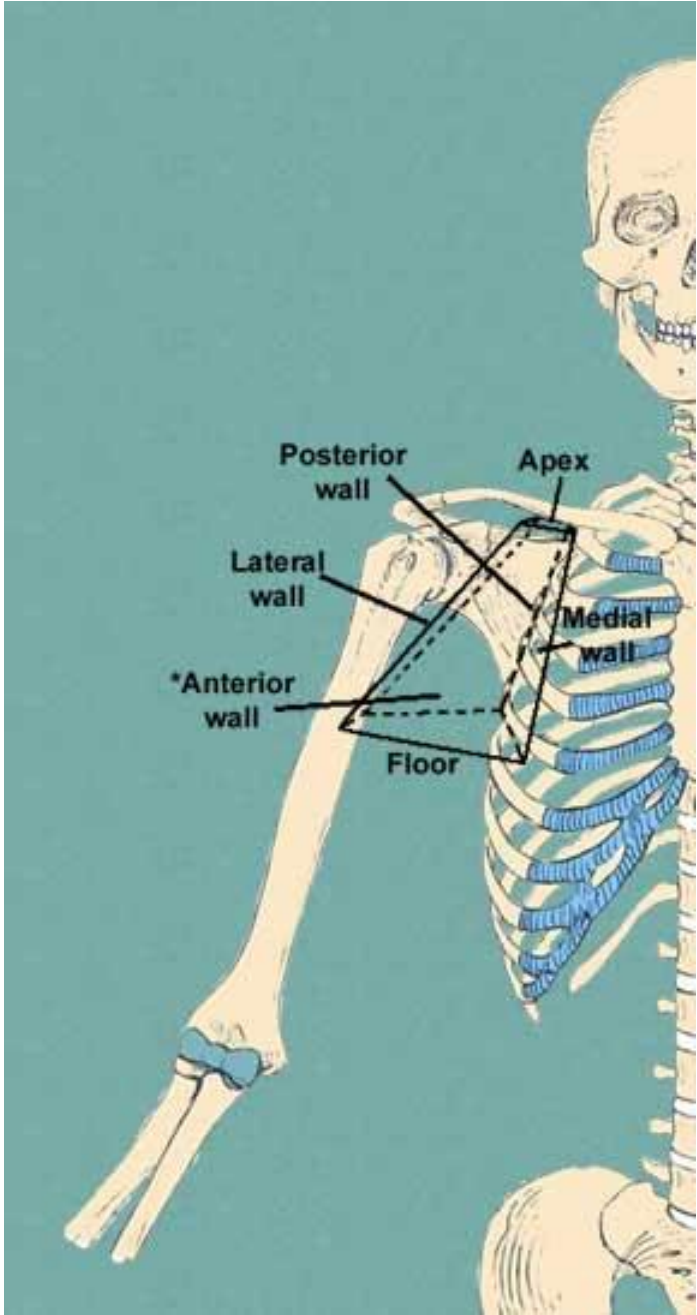
Harun NH, Taib NA, Yip CH. Is clinical assessment of the axilla a reliable indicator for lymph node metastases in breast cancer? ANZ J Surg 2008 Nov;78(11):943-4.

Predictors of LN metastases

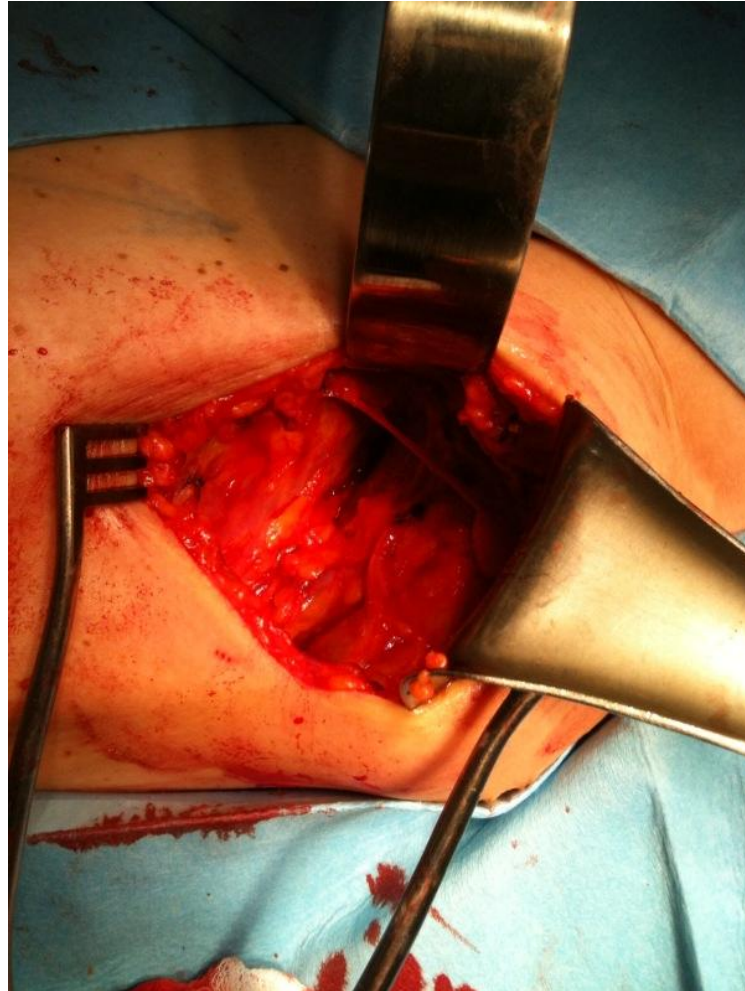
- Predictors of axillary node metastases have been studied.
- In T1 tumors, the reported incidence of lymph node metastases ranges from 21% to 35%.
- Primary tumor characteristics can be used to identify a subgroup of patients with a low risk of axillary lymph node metastases in T1 breast cancer, such as **grade, size, lymphovascular invasion and a low Ki-67 staining**, and preoperative risk assessment might be used to omit routine axillary lymph node dissection in those patients at low risk of axillary lymph node metastases

Objective

1. To evaluate the incidence and predictors of axillary lymph node metastases in patients with breast cancer.
2. To identify a selected group of patients where axillary dissection can be safely omitted







Extent of axillary dissection

- Level 1 – nodes lateral to pectoralis minor
- Level 2 – nodes under pectoralis minor
- Level 3 – nodes medial to pectoralis minor to the costoclavicular ligament
- Superiorly fat cleared in front of and below the axillary vein
- Previously intercostobrachial nerve is routinely divided – currently recommendations are that it should be preserved whenever possible to preserve sensation in the axilla and inner arm
- Level 1-3 is a full clearance
- The term sampling is imprecise and should not be used
- Low axillary clearance indicated for DCIS - up to level of intercostobrachial nerve

Audit of axillary dissection - UMMC

- Retrospective study of 953 patients with **T1 and T2 invasive breast carcinomas** seen in the University Malaya Medical Centre between Jan 2001 to Dec 2005.
- This comprised 60.5% of the total 1574 women newly diagnosed with breast cancer during the same period.
- Axillary dissection was done for all the patients.
- Factors such as **age, size of tumour, grade, and lymphovascular invasion**, all of which were derived from the histopathology report, were studied in relation to nodal involvement, and binary logistic regression analyses was carried out to determine the independent predictors of axillary node metastases by univariate and multivariate analysis.

Yip CH, Taib NA, Tan GH, Ng KL, Yoong BK, Choo WY. Predictors of axillary lymph node metastases in breast cancer: is there a role for minimal axillary surgery. World J Surg. 2009 Jan;33(1):54-7.

Type of Surgery

Type of Surgery	Number	%
Breast conservation Surgery	283	29.7%
Mastectomy	670	70.3%
TOTAL	953	100%

Race and Age Incidence

Age in years	Malay	Chinese	Indians	Others	TOTAL
<30	1	10	3	0	14
30-49	90	304	47	8	449
50 and above	64	361	62	3	490
TOTAL	155	675	112	11	953

No of Lymph Nodes Involved

No of Nodes	No of patients	Percentage
1-3	217	59.5%
4-9	87	23.8%
10 or more	61	16.7%
TOTAL	365	100%

Factors affecting LN positivity

		Total no	No positive nodes	P value
Age	<50	463	186 (40.1%)	0.129
	50 and above	490	179 (36.1%)	
Grade	1	92	22 (23.9%)	0.00
	2	438	180 (42.5%)	
	3	277	121 (43.9%)	
LVI	None	447	109 (24.4%)	0.00
	Present	322	168 (52.2%)	

Size and Lymph node involvement

		Total no	Lymph nodes involved	P value
SIZE	T1a >0.1-0.5 cm	13	1 (7.7%)	0.00
	T1b >0.5-1 cm	65	8 (12.3%)	
	T1c >1-2 cm	346	101 (29.2%)	
	T2 >2- 5 cm	529	255 (48.2%)	

Conclusion from this study

- For T2 tumours, where 48.2% have nodal metastases, a full axillary clearance should be carried out.
- However in T1 tumours, only 25.9% have nodal metastases, and axillary dissection will be overtreating almost three quarters of the patients.
- In T1a tumours nodal metastases is only 7.7%, while in . T1b and T1c tumours, the incidence of nodal metastases is 12.3% and 29.2% respectively. In these cases, a sentinel lymph node biopsy is justified.

Association between Ethnicity and Lymph Node Metastasis in South East Asian Women

	Ethnicity			P value
	Chinese	Malay	Indian	
Tumor size less than 2 cm (N = 937)				0.005
No nodal involvement, N (%)	568 (77.0)	84 (64.6)	57 (82.6)	
Lymph node involvement, N (%)	170 (23.0)	34 (41.0)	12 (17.4)	
Adjusted odd ratio ^a	1.00	1.57	0.64	
95% confidence interval		(1.05-2.37)	(0.33-1.24)	

^a Logistic regression model adjusted for tumor size (continuous), tumor grade, estrogen receptor status, and progesterone receptor status

*Bhoo Pathy N, Hartman M, Yip CH, Taib NA, Saxena N, et al.
Cancer Res 2010;70(24 Suppl): 289 s*

Association between Ethnicity and Lymph Node Metastasis in South East Asian Women

	Ethnicity			P value ^b
	Chinese	Malay	Indian	
Tumor size 2 to 5 cm (N = 2228)				0.028
No nodal involvement, N (%)	865 (53.8)	160 (43.7)	125 (49.0)	
Lymph node involvement, N (%)	742 (46.2)	206 (56.3)	130 (51.0)	
Adjusted odds ratio ^a	1.00	1.45	1.18	
95% confidence interval		(1.15-1.84)	(0.89-1.55)	

^a Logistic regression model adjusted for tumor size (continuous), tumor grade, estrogen receptor status, and progesterone receptor status

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- Grade, size and presence of lymphovascular invasion was significantly related to lymph node involvement.
- Sentinel lymph node biopsy, utilizing the radionuclide and blue dye together is an expensive procedure which costs USD200 per patient just for the disposables alone, and is probably not justified for T2 tumours where 48.2% have nodal metastases.
- But in T1 tumours where 25.9% have nodal metastases, it can avoid a complete axillary dissection in almost three-quarters of the patients.
- In T1a tumours where nodal metastases is only 7%, axillary surgery can be omitted especially in a low-grade tumour with no lymphovascular invasion.

Conclusion

- Predictors of axillary lymph node metastases are size and grade of tumour, and the presence of lymphovascular invasion.
- Ethnicity also appear to have an impact on LN metastases, esp in small tumours
- Minimal axillary surgery is safe in a T1 tumour with a low grade and absence of lymphovascular invasion.